Concept of Chronopharmacology w.s.r. Aushadha Sevana Kala in Ayurveda

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ABSTRACT
Chronobiology is the science which deals with the biological rhythmic phenomenon in the living system. Chronopharmacology is the branch of Chronobiology which deals with the Pharmacologic aspects of Chronobiology. In Ayurveda, Aushadha Sevana Kala is the proper time of administering the aushadha (medicine). The proper knowledge of Agni (digestive fire) and Aushadha Sevana Kala (time for drug administration) will help in understanding the food and drug interaction which is helpful in the proper treatment of a patient. In different Ayurvedic texts, Acharyas had defined Aushadha Sevana Kalas according to the biological clock for attaining the equilibrium between the Doshas and Dhatus which ultimately leads to swasthya (good health). The present article is an attempt made to have a Critical Study of different Aushadha Sevana Kala in Ayurveda with special reference to Chronopharmacology.

KEYWORDS
Chronobiology, Chronopharmacology, Circadian Rhythms, Aushadha Sevana Kala, Charaka, Sushruta, Ashtanga Hrudaya, Sharangadhara
INTRODUCTION
Chronopharmacology is the study of how the effects of drugs vary with biological rhythms and endogenous periodicities. In early 1970, the term Chronopharmacology had been recognized as a scientific domain of investigation. Chronotherapeutics refers to a treatment method in which in vivo drug availability is timed to match with biological rhythms of disease, in order to gain best therapeutic outcomes and minimum side effects. Until the 20th Century, Modern Science was not much aware of the biochemical, physiological and pathological variations of human body within 24 hour period. But the Ayurvedic texts had very well described the pharmacokinetics and pharmacodynamics of medicine under the umbrella of Aushadha Sevana Kala which is directly affected by biological rhythmic activities of the body.

The Circadian clock controls the biological rhythm of our body. Circadian rhythms are self-sustaining endogenous oscillations occurring in a period of 24 hours. The normal sleep-wake cycle is related to the circadian rhythms of human body. These rhythms are under the controlled by Suprachiasmatic nuclei (SCN) that are situated in the hypothalamus and the pineal gland. This master clock network regulates the circadian clocks located in cells, tissues, and organ-systems. The chronopharmacologic approaches tend to reduce the side effects and to make the drug more bio-available. The approach of conventional homeostatic is replaced by the proper study of Chronopharmacology. The Chronopharmacological principle is very well applied in the therapy of Myocardial Infarction (MI), diabetes, hypercholesterolemia, bronchial asthma, arthritis, hypertension etc.

Kala (time) is unavoidable and unique, it is the specific causative factor for all type of effects. That is why, Ayurveda being the science of life, gives emphasis on the concept of Kala (time). The Aushadha (medicine) and Kala (time) relationship are explored by our ancient Acharyas. According to Acharya Vagbhata, Kala (time) fulfills the aim of administration of Aushadha (medicine) which is rightly stated as ‘Kalo Bhaisajya Yoga Krt’. In the same context, Acharya Charaka says that Aushadha (medicine) 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.
When to intake the aushadha i.e. before or after or in between the meals or at night depends upon the disease and medicine itself. The basic knowledge of the concept of Aushadha Sevana Kala in the day to day practice is very important to treat patients more accurately and effectively. Though Kala (time) has relationships with all the effects, to prove it the present study is designed to understand the chronopharmacology with special reference to Aushadha Sevana Kala.

AIMS AND OBJECTIVES
The present study has been undertaken with following aims and objectives.
1. To study the Aushadha Sevana Kala from different classical Ayurvedic texts.
2. To understand the concept of Aushadha Sevana Kala in detail.

MATERIAL AND METHODS
The classical Ayurvedic texts have been used as a material for this study. The important books from which various references have been collected in this study are Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya, Astanga Sangraha, Sharangadhar Samhita and available commentaries on these Samhitas.

LITERATURE REVIEW
The following Ayurvedic texts have elaborated the concept of Aushadha sevana kala.
2. Sushruta Samhita Uttara Tantra – Swasthavritta Adhyaya².
5. Sarangadhara Samhita Purvakhanda – Bhaishajyakhyanakam adhyaya⁵.

The total number of Aushadha Sevana Kala are different according to different Ayurvedic texts [Table 1]. The importance of Aushadha Sevana Kala in disease management has been classified as below as follows.

1. Abhakta /Niranna kala (Empty stomach)⁷.

Indications:
- Patient with good digestive fire (Pradipta Agni Avastha)
- Patients having a good strength (Balwan Rogi) and with Balavan Vyadhi.
- Administered as Rasayana.
- Kapha Vikaras (Kaphaja disease)
• **Pitta / KaphaVruddhi** (increase) and for intake of *Vamana-Virechana Aushadhi*.

**Contraindications:**
- Children (*Bala*), Pregnancy (*Garbhini*), Female (*Stree*) patient
- **Depletion of Dosha and Dhatu** (*Doshakshaya, Dhatukshaya*).

**Action of Bheshaja**
Ayurvedic scholars adopt this *breshaja kala* because the potency of medicine and interaction between *Aushadha* and digestive fire (*Agni*) is not hindered by food. *Hemadri* suggests that *Aushadha* should be given once the consumed food is digested and after digestion of *aushadha*, food is given. According to *Indu*, *Aushadha* should be given on empty stomach, but two hours after sunrise because in this *kala*, *Amashaya* and *Strotasas* are devoid of *Kapha*.[Table 3,4]

2. **Pragbhakta/ Bhuktadau (Before Meal)**
*Pragbhakta* means before meals. In this specific *Aushadha kala*, *Hemadri* suggests taking *Aushadhi* immediately followed by food.[Table 1].

**Indications**
- **Apanavayu Vikruti**
- Diseases of lower (*Adha*) body (*Kaya*) diseases (*Vikaras*)
- **Mutravaha-Malavaha-Shukravaha Strotasas**,  
- **Pakvashayagata Vyadhi**,  
- **Arsha, and Gudabhransha.**  
- **Meda vikruti**(fat).

3. **Madhyabhaqta (In between meals)**
In this *Aushadha sevana Kala*, the *Bheshaja* is administered in between the meal. According to *Chakrapani* and *Indu*, the half portion of the food is taken initially, followed by *Aushadha* administration, and again followed by the remaining portion of food.[Table 2,3,4].

**Indications**
- **Samanavayu Vikruti.**  
- **Mandagni**  
- **Koshthagatavyadhi,**  
- **Pakvashayagata Vyadhi, Shula, Gulma,Grahani.**  
- **Paittika Vikaras (disease),and**  
- **Strotoressdhanashak.**  

**Action of Bheshaja**
The food restricts the *Urdhwagati* and *Adhahgati* of *Aushadha* and hence it is forced to act locally. Therefore helps to cure *Sthanik Doshas* as *Samana Vayu* and *Pachaka Pitta* are both situated in the *Koshtha*.

4. **Pashchadbhakta/ Adhobhakta (after Lunch & Dinner)**
In this *kala*, *Bheshaja* is administered after meals (after lunch and Dinner). According to *Cakrapani Pashchadbhakta kala* is for both morning and evening time after meals. *Hemadri* and *Indu*, further added...
that Bheshaja is to be administered immediately after meals [Table 2, 3, 4].

**Indications**
- In Vyana vayu vikruti, Bheshaja is administered after lunch.
- In Udana vayu vikruti, Bheshaja is administered after dinner.
- Vyanavayujanya vikruti - Jvara, Shopha, Napunsakata (debility), Udasinta (depression), bodyache, tingling, numbness, Kushtha, Visarpa.
- Udanavayujanya vikruti - Gala vikar, Aruchi, Chhardi, Pinasa, Galaganda, Urdhvajatrugata Vyadhi, Karshya, Ura Sthangata Kasa – Shwasagata Vyadhi

**Action of Bheshaja**
- After lunch- stimulation of Vyana Vayu. It is considered as Ura – Urdhva jatrugata, Bala (strength) Vruddhikara (increase) Aushadha Sevana kala, Kapha Dosha Janya Vyadhi, Pushti (strength) janya Aushadhi Sevana – Sarvottam Kala.
- After dinner- stimulation of Udana Vayu. It is considered as Udanavayu causes the Urdhvagati of Bheshaja, it strengthens the upper part of body (urdhwaanga), especially the sense organs.

5. **Muhurmuhu (frequently administered)**

In this Aushadha Sevana Kala, Aushadha is administered frequently regardless of Bhukta or Abuktavastha is Muhurmuhu Kala [Table 3, 4, 5]. Except Chakrapani, all authors opinion that Aushadha should be given irrespective of meals [Table 2].

**Indications**
- Pranavahastrotogata Vyadhi--Shvasa, Kasa, Hikka
- Udakavahastrotogata Vyadhi – Pipasa Vikara.
- Annavahastrotogata Vyadhi – Chhardi, Vishbadha.

**Action of Bheshaja**:-
- In this Aushadha Sevana kala the medicine is administered in Atyayika (Emergency life-threatening) diseases which need immediate therapeutic intervention.
- Sublingual absorption provides faster relief and High concentration of drug provides more bio-availability which treats the vitiated doshas in their Sanchaya & Vegavastha.

6. **Samudga (Before food and after food)**

Samudga means before and after food. Food taken should be Laghu (light).

**Indications**
- In Hikka, Kampa, Aakshepaka and Adha (lower) kaya (body) vikara (disease),
- In Vyana, Apana, and Udana Vayu Vikruti.
• In Vataja Prameha and Shukradosha.

**Action of Bheshaja**

Aushadha is administered at the time immediately before and after meals. All commentators are unanimous about Samudga Kala i.e. Aushadha to be given before and after meals. Indu and Hemadri specify that Aushadha should be consumed immediately in relation to food[Table 2,3,4].

7. **Sabhakta (mixed with food)**

Sabhakta kala means Aushadha is given mixed with food. All the commentators agree that Aushadha should be consumed along with food but Indu opines that Aushadha is processed or cooked or it is given along with the food[Table 3,4].

**Indications**

• It is indicated in SukumaraVyakti, Bala (Child),
• In Aruchikara (unpalatable) Aushadha.
• In Sarvangata (whole body) Vikara.

**Action of Bheshaja**

The drug mixes with Rasadhatu & then spreads all over the body through Urdhva-Adha and Tiryak Gati. Therefore useful in Sarvangasamshrita vyadhis.

8. **Sagrasa (with each and every morsel of food)**

Sagrasa Aushadha kala means aushadha is given with each and every morsel of food. All authors have same opinion regarding this kala.

**Indications**

• It is indicated in Prana Vayu Dushtijanya Vikara (Respiratory diseases like Pinasa, Ardita, trusha, Shvasa).
• In Hrudroga,
• Indicated as Dipana- to stimulate agni,
• Bheshaja- Vajikarana Bheshaja (Churna, Leha, Deepana Dravya, Vati, Gati)

**Action of Bheshaja**

In normalcy, Pranavayu regulates the intake of food. In Grasa Kala, Bheshaja stimulates the Pranavayu. So the Indriyaprasadana & Chittaprasadana takes place. This enhances the Vrishya Prabhava of the Vrishya Dravyas[Table 2,3,4].

9. **Grasantara (in between two morsel of food)**

In Grasantara Aushadha sevana kala means bheshaja is administered in between two morsels of food.

**Indications**

• It is indicated in Prana Vayu janya Vikara (Pinasa, Ardita, Trusha, Shvasa)
• In Hrudroga².
• Prana Vayu Prakopavastha.
• Indicated for Vamana dravya.
• Indicated for Kasaghna dhuma.

**Action of Bhesjaha**

Normal Pranavayu regulates the intake of food. In Grasantara Kala, Bhesjaha stimulates the Pranavayu. So the Indriyaprasadana & Chittaprasadana takes place. This enhances the Vrishya Prabhava of the Vrishya Dravyas [Table 2,3,4].

**10. Nisha (Before sleep)**

Nisha aushadha sevana Kala means medicine is administered after digestion of food consumed. Indu specifically defines the Nisha Kala as the time after the evening meal has digested and 3 hours have been passed. Sharangadhara has mentioned it is an Anannavastha [Table 4,5].

**Indications**

- It is indicated in Urdhvajatrugata Vikara (disease),
- Indicated for Vamana, Dhumapana.

**Action of Bhesjaha**

The purpose of this kala is for Anulomana and Brimhana. In this kala, Bhesjaha specifically acts on Urdhvajatrugata parts. The Bhesjaha gives Chiraparinamama prabhava (long lasting action) of the Shamana Aushadhi as no food intake occurs until the next morning.

**11. Antarbhakta (after digestion of meal in noon)**

In this Bhesjaha kala, Aushadha is to be intaken in Madhyanha, when the previous consumed food is digested and after Aushadha is metabolised, again food is to be taken in the evening [Table 1].

**Indications**

- It is indicated in Diptagni Vikara (diseases) and
- In Vyana Vata Dosha Janya Vikara (disease).

**Action of Bhesjaha**

Due to madhyanha i.e. Pittakala, Agni is in a stimulated condition. So Bhesjaha is properly metabolized in this kala. In this kala Aushadha shows Hrudya, Pathya, Deepana and Manobalakara effect [Table 3,4].

**Table 1** Types of Aushadha Sevan Kalas as per different Samhitas

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Charaka</th>
<th>Sushruta</th>
<th>Ashtanga Sangraha</th>
<th>Ashtanga Hrudaya</th>
<th>Sharangadhar a Samhita</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pratah Niranna</td>
<td>Abhakta</td>
<td>Abhakta</td>
<td>Abhakta</td>
<td>Suryodayajatha</td>
</tr>
<tr>
<td>2</td>
<td>Bhuktadu</td>
<td>Pragbhakta</td>
<td>Pragbhakta</td>
<td>Pragbhakta</td>
<td>Divasabhojan e</td>
</tr>
<tr>
<td>3</td>
<td>Bhuktamadhye</td>
<td>Madhyabhakta</td>
<td>Madhyabhakta</td>
<td>Madhyabhakta</td>
<td>Sayambojane</td>
</tr>
<tr>
<td>4</td>
<td>Bhuktapaschhat</td>
<td>Adhobhakta</td>
<td>Adhobhakta</td>
<td>pushchadhakta</td>
<td>Muhurmuhu</td>
</tr>
<tr>
<td>5</td>
<td>Bhaktasanyukta</td>
<td>Sabhakta</td>
<td>Samabhakta</td>
<td>Sabhakta</td>
<td>Nishi</td>
</tr>
</tbody>
</table>
### Table 2 Aushadha Sevana Kala according to Charak Samhita

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Aushadha Sevana Kala</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pratah Niranna</td>
<td>Ballwanarugna Durbararugna</td>
</tr>
<tr>
<td>2</td>
<td>Bhuktaadu</td>
<td>Apana vayu vikruti</td>
</tr>
<tr>
<td>3</td>
<td>Bhuktamadhye</td>
<td>Samana vikruti</td>
</tr>
<tr>
<td>4</td>
<td>Bhuktapaschat – Pratah</td>
<td>Vyana vayu vikruti</td>
</tr>
<tr>
<td>5</td>
<td>Bhuktapaschat – Sayam</td>
<td>Udana vayu vikruti</td>
</tr>
<tr>
<td>6</td>
<td>Bhaktasanyukta</td>
<td>Aruchi</td>
</tr>
<tr>
<td>7</td>
<td>Muhurmuhu</td>
<td>Shwasa-Kasa-Pipasa</td>
</tr>
<tr>
<td>8</td>
<td>Samudga</td>
<td>Hikka</td>
</tr>
<tr>
<td>9</td>
<td>Sagrasa</td>
<td>Prana vayu vikruti</td>
</tr>
<tr>
<td>10</td>
<td>Grasantara</td>
<td>Prana vayu vikriti</td>
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</tbody>
</table>

### Table 3 Aushadhi Sevana Kala according to Sushruta Samhita

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Aushadhi Sevana Kala</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abhakta</td>
<td>Sukumar, bala, vriddha</td>
</tr>
<tr>
<td>2</td>
<td>Pragbhakta</td>
<td>Bala, vriddha, sukumar</td>
</tr>
<tr>
<td>3</td>
<td>Madhyabhakta</td>
<td>Koshtha gatyadhi</td>
</tr>
<tr>
<td>4</td>
<td>Adhobhakta</td>
<td>Urdhva sharirgata vyadhi Balya</td>
</tr>
<tr>
<td>5</td>
<td>Sahbhakta</td>
<td>Mano balvardhaka, deepana</td>
</tr>
<tr>
<td>6</td>
<td>Antarabhakta</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Muhurmuhu</td>
<td>Hikka, shwasa, kasa, vaman</td>
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<tr>
<td>8</td>
<td>Samudga</td>
<td>Urdhvaagami and adhogami dosha</td>
</tr>
<tr>
<td>9</td>
<td>Grasa</td>
<td>Vajikarana</td>
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<tr>
<td>10</td>
<td>Grasantara</td>
<td>Mandagni</td>
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### Table 4 Aushadhi Sevana Kala according to Ashtang Sangraha

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Aushadhi Sevana Kala</th>
<th>Indications</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Abhakta</td>
<td>Swastha purusha (Healthy person)</td>
</tr>
<tr>
<td>2</td>
<td>Pragbhakta</td>
<td>Apanavikruti, Shoulyyata</td>
</tr>
<tr>
<td>3</td>
<td>Madhyabhakta</td>
<td>Samanavikruti, koshthagataroga, Pittajaroga</td>
</tr>
<tr>
<td>4</td>
<td>Adhobhakta</td>
<td>Urdhvajatrugataroga</td>
</tr>
<tr>
<td>5</td>
<td>Samabhakta</td>
<td>Sarvagavyadhi</td>
</tr>
<tr>
<td>6</td>
<td>Antarabhakta</td>
<td>Vyanavyadhi</td>
</tr>
<tr>
<td>7</td>
<td>Muhurmuhu</td>
<td>Hikkashwasa, kasa, trusha, chhardi, Vishaktata.</td>
</tr>
<tr>
<td>8</td>
<td>Samudga</td>
<td>Hikka, kampa, aakshepa Urdhwa / Adhaparshwa vyadhi</td>
</tr>
<tr>
<td>9</td>
<td>Sagrasa</td>
<td>Prana vayu vikruti vajikarana</td>
</tr>
<tr>
<td>10</td>
<td>Grasantara</td>
<td>Pranavayu vikriti, hrudroga</td>
</tr>
<tr>
<td>11</td>
<td>Nishi</td>
<td>Urdhva jatru gata vyadhi, vaman, dhumapana</td>
</tr>
</tbody>
</table>

### Table 5 Aushadhi Sevana Kala according to Sarangadhara Samhita

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Aushadhi Sevana Kala</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Suryodayajatah</td>
<td>Pitta / kaphajavyadhi, Virechana Vamana Lekhana</td>
</tr>
</tbody>
</table>
Vaidyas largely accepted the nomenclature described by Acharya Charaka. The ancient texts of Ayurveda have described 10 types of Aushadha Sevana Kalas (time). The texts differ about the nomenclature of Aushadha Sevana Kalas (time) [Table 1]. In Niranna Kala the aushadha is administered in empty stomach. Agni and Aushadha interaction is unobstructed because of absence of food. Agni (digestive fire) should be Pradipta (increased) for this Kala. Although Aacharya Charaka and Vaghbhata told the more number of Bheshaja Sevana Kala, but they can be incorporated in Bheshaj Sevana Kala told by Aacharya Sharangdhara. Abhakta, Pragbhakta and Bhaktadau can be included in Suryodayajataha. Madhyabhakta, Adhobhakta (after morning meal), Antarabhakta, Samudga (before and after morning meal) can be included in Divasa Bhojane. Adhobhakta (after evening meal), Samudga (before and after evening meal), Grasa, Grasantara can be included in Saayam Bhojana. [Table 5]

Aushadha Sevana Kala is said to be the specific time for drug administration. Aushadha Sevana Kalas were widely accepted by the Ayurvedic Scholars for being its importance in shodhana and samana chikitsa. The ten Aushadha sevana kala of Charak, Sushruta and Ashtanga Hrdaya and eleven of Ashtanga Sangraha are well incorporated into five Aushadha Sevana Kala of Sharangadhara. In Ayurveda, Aushadha Sevana Kalas are described in relation to food only and the route of administration to is specified to oral route. The specific Kala(time) for Aushadhi (drug) sevana (administration) is very important as it has direct impact on treatment success. 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. Chronopharmacology and Chronotherapeutics has emerged an important area for research for medical fraternity as its correct knowledge helps Vaidya to treat patient more effectively. Hence the success of treatment always depends upon the time of drug administration.
REFERENCES