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Chronotherapeutics in *Ayurveda*

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ABSTRACT

In order to maximize health benefits and minimize adverse effects of a treatment, chronotherapeutics is administered to patients according to his/her daily, monthly, seasonal or yearly biological clock. According to *Ayurveda* observation of the specific features of disease corresponding to season, day and night, age and meal is known as *Kaala Aveksha*. The *Dasha Bheshaja Kaala* (ten different time period for the administration of medicine) is one among the *Shadaveksha Kaala* (Six observatory aspects of time). It is defined according to the biological clock. The medicines at proper *Bheshaja Kaala* help to attain the equilibrium of *Doshas* and *Dhatu*s. Here chronotherapeutics can be correlated with *Bheshaja Kaala*. As it gives importance to the time of administration which can be responsible for variations of drug kinetics. **Objective:** To conduct an in-depth analysis of the literature in order to identify and evaluate the evidence base for chronotherapy. **Data source:** A literature search was conducted in classics of *Ayurveda* and electronic databases. **Result:** Review shows that the drug administered according to the *Bheshaja kaala* has more beneficial outcomes than the other methods. **Conclusion:** The review presents the scope of chronotherapy in drug administration.

Key words: *Aushadhakaala, Bhaishajya Kaala, Bheshaja Kala, chronobiology, chronotherapy.*

INTRODUCTION

Biological rhythms are sequences of events that are repeated over time in the same manner and with the same interval such as circadian, ultradian, infradian, circannual regulates many body functions in humans. Many diseases like hypertension, asthma, peptic ulcer, cancer follow these rhythms. Blood pressure and heart rate are highest during the hours of 6am-12pm. Human synchronizers can be knowledge of the time of day, light-dark cycle, sleep-wake cycle, time of

eating. Use of these rhythmic cycles for the application of therapy is chronotherapy, the science of time related medication. It is administered to maximize the desired effects and to minimize the undesired effects of a treatment. Chronotherapy can be classified in to time controlled systems where in the drug release is controlled primarily by the delivery system, stimuli induced pulsative drug delivery system in which release is controlled by the stimuli, such as P^H or enzymes present in the intestinal tract.^[1]

The safety and efficacy of the drug is achieved by coordinating the peak plasma concentration of the drug with circadian rhythm of the body.^[2] Some of the examples for circadian time-dependent changes in the pharmacokinetics of medications are the cardiovascular active drugs such as beta-blockers, calcium channel blockers, ACE-inhibitors, organic nitrates etc, anti-asthmatics drugs like theophylline, beta agonists, leukotriene antagonists, glucocorticoids etc, anticancer agents such as 5-FU, methotrexate, 6-mercaptopurine, platinum analogues etc, NSAIDs, local anaesthetics, H1 and H2-histamine antagonists,

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protein pump inhibitors, antidepressants and such other central nervous system acting drugs.^[3]

Ancient scholars of *Ayurveda* have documented environmental influence on human physiology as the functioning of *Tridosha* (3 humours) as which are responsible for the normal functioning of the body. The physiological variation of *Tridosha* depends on the factors like *Vaya* (age), *Ahas* (day), *Ratri* (night), *Bhukta* (intake of food)^[4] which all are related to time. The pathological vitiation of the *Dosha* leads to disease and its intensity will be more during the physiological dominant time of each *Dosha*. So, the administration of the medicine at the dominant phase will lead to the pacification more effectively. Observation of the specific features of disease corresponding to season, day and night, age and meal is known as *Kaala Aveksha*.^[5] The concept of *Bheshaja Kaala* mentioned by *Ayurvedic* scholars is one among the *Shad Aveksha Kaala* (Six observatory aspects of time) like 1) *Dina* (day) 2) *Rogi* (patient) 3) *Aushadha* (medicine) 4) *Vyadhi* (disease) 5) *Jeerna Lakshana* and 6) *Rutu* (seasons).^[6] The administration of *Bheshaja* (medicine) is mainly related to the day, afternoon, evening and night time with relation to timing of food. Because the rhythm of *Tridosha* varies according to this time as *Vatika* disorders aggravate at the end of day, end of night and after digestion. *Pittaja* disorders in the middle of the day, middle of night, and during digestion and *Kaphaja* disorders in the beginning of the day, beginning of the night, and just after meals.^[7-8] Similarly the rate of metabolism of drug with the help of *Agni* (digestive fire) is also affected by the factors like food, type of drug, time of drug administration. *Agni* (digestive fire) present in the *Jathara* (stomach) which digests the food and drug is served by *Prana*, *Apana* and *Samana Vata* by blowing/increasing, protecting and preserving. Hence success of treatment depends on proper administration of drugs which includes appropriate dosage and timing.^[9]

MATERIALS AND METHODS

The review data was collected from *Ayurvedic* classics like *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Sangraha*, *Kashyapa Samhita*, *Sharangadhara*

Samhita, and the electronic databases like Google scholar, pub med, Scopus and Google for relevant studies. Search revealed total 5243 articles of which 83 articles were selected. Among 83 articles, references from abstracts and full-text articles which are freely downloadable and relevant for this were only included.

REVIEW OF LITERATURE

According to *Ayurveda*, *Chikitsa Kaala* (treatment time) depends up on 1) *Dina* (day) 2) *Rogi* (patient) 3) *Aushadha* (medicine) 4) *Vyadhi* (disease) 5) *Jeerna Lakshana* and 6) *Rutu* (seasons) together called as *Shad Aveksha Kaala*.

***Dina* (different parts of the day):** It indicates particular part of the day, for example, *Vamana Dravya* (emetics) is to be given in the early morning, that is *Purvahna* (morning).^[10]

***Rogi* (patient):** After assessing the strength of the patient, time of administration for medicine should be selected. If a patient has good strength, then medicine can be given in empty stomach early in the morning and if the patient is weak, medicine should be administered after *Laghu Bhojana* (light food).^[11]

***Vyadhi* (disease):** Based on the *Vyadhi* (disease) also *Kaala* is classified. For example: In *Jwara* (fever)-every 6th day the medicine has to be changed like *Peya* (liquids), *Kasaya* (decoctions), *Kshira* (milk preparation), *Sarpi* (ghee preparation) and *Virechana* (purgation) respectively depending on the condition.^[12]

***Jeernalinga* (stage of the digestion of the food):** The *Jeerna Lakshanas* (digested signs) like proper appetite, timely discharge of urges (flatus, faeces, urine etc.), lightness of the body and feeling of purity of eructation should be assessed before administering the medicine. If the *Bheshaja* (medicine) is administered in *Amavastha* (undigested stage) and *Jiryamana Avastha* (during digestion) it produces the aggravation of symptoms.

***Ritu* (nature of the season):** Based on the *Ritu*, *Kaala* should be assessed by *Chaya* (increase of *Dosha* on site), *Prakopa* (excessive increase of *Dosha*) *Lakshanas*

told for each *Dosha* and administer medicine accordingly.^[13]

Aushadha (medicine): Based on the type of medicine, *Kaala* have been told. The time of administration and the type of medicine must be decided as per the condition and diseased status of the patient.

Appropriate timing of drug administration in relation to *Kaala Aveksha* is a complex process. But the administration of the medicine at the dominant phase of *Dosha* will leads to the pacification more effectively. Classical references of some diseases that shows the rhythmicity described in table 1.

Table 1: Examples for disease which shows rhythmicity

Diseases	Rhythmicity
<i>Vataja Shophya</i> (inflammatory edema due to <i>Vata Dosha</i>). ^[14]	Aggravates during day time
<i>Kaphaja Shophya</i> (inflammatory edema due to <i>Kapha Dosha</i>). ^[15]	Aggravates at night

<i>Sangraha Grahani</i> (colitis). ^[16]	Aggravates during day and relieves at night.
<i>Vataja Shiroroga</i> (headache due to <i>Vata Dosha</i>). ^[17]	Intensity of head ache maximum at night
<i>Pittaja Shiroroga</i> (headache due to <i>Pitta Dosha</i>). ^[18]	Intensity of headache is alleviated at night
<i>Sooryavarta</i> (headache at supra orbital region). ^[19]	Headache starts with the sunrise, its intensity gradually increases with and maximum in mid noon, then its intensity diminishes gradually.

According to *Ashtanga Sangraha* the time of administration of medicine are 11 in number. In *Samhitas* like *Charaka*, *Susrutha*, *Ashtanga Hrudaya* and *Kashyapa* 10 types of *Bheshajakaala* are explained. *Sarangadhara* included this under five *Bheshaja Kaala*. Types of *Bheshaja Kaala* are described in table 2.

Table 2: Bheshaja Kaala according to different Acharyas

SN	<i>Charaka Samhita</i> ^[20]	<i>Susruta Samhita</i> ^[21]	<i>Ashtanga Sangraha</i> ^[22]	<i>Kasyapa Samhita</i> ^[23]	<i>Sharangadara Samhita</i> ^[24]
1.	<i>Niranna</i>	<i>Abhakta</i>	<i>Abhaktam</i>	<i>Poorvebhaktasya</i>	<i>Prabhate</i>
2.	<i>Bhuktadau</i>	<i>Pragbhaktm</i>	<i>Pragbhaktam</i>	<i>Madyebhaktam</i>	<i>Divasabhojane</i>
3.	<i>Bhuktamadye</i>	<i>Madyebhaktm</i>	<i>Madyebhaktam</i>	<i>Adhobhaktam</i>	<i>Saayantanebhojane</i>
4.	<i>Praatabhakta</i>	<i>Adhobhaktam</i>	<i>Adhobhaktam</i>	<i>Saamudgam</i>	<i>Muhurmuhu</i>
5.	<i>Paschat</i>	<i>Muhurmuhu</i>	<i>Sabhaktam</i>	<i>Muhurmuhu</i>	<i>Nisi</i>
6.	<i>Sayambhaktapaschat</i>	<i>Samudgam</i>	<i>Antarabhaktam</i>	<i>Sabhaktam</i>	-
7.	<i>Muhurmuhu</i>	<i>Sabhaktam</i>	<i>Samudgam</i>	<i>Bhaktayormadyam</i>	-
8.	<i>Samudgam</i>	<i>Grasantaram</i>	<i>Muhurmuhu</i>	<i>Graasa</i>	-
9.	<i>Bhakta Samyuktam</i>	<i>Antarabhaktam</i>	<i>Sagrasam</i>	<i>Grasaantara</i>	-
10.	<i>Grase</i>	<i>Grase</i>	<i>Grasantare</i>	<i>Abhakta</i>	-

11.	Grasantaram	-	Nisi	-	-
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Aushadha Sevana Kaala explained by different *Acharyas* can be incorporated as per *Ashtanga Sangraha*

Abhakta (Without giving any food) - In persons who are strong, drugs should be given in the morning after the increased *Kapha* has moved out of the *Koshta*. In case of others, it should be before food (of the morning or breakfast) as the person will not suffer from fatigue by the support of food. This is very potent; it eradicates all the disease immediately as the strong person defeats the weak,^[25] however if it is used by children, aged, women and weak person it causes languor and loss of strength.^[26] *Pratah Niranna Kaala* is specified by *Charaka*. *Chakrapani* considered it as *Bhuktadau Kaala*.

Pragbhakta (Just prior to the meal) - *Hemadri* states that in this *Kaala* the *Bheshaja* intake is immediately followed by food. It is useful in the treatment of disease caused by *Apana Vata*, in diseases of the lower extremities, for strengthening the body and for making the body thin. The medicine used before food does not cause loss of strength, it destroys the *Doshas* located in stomach, it gets digested immediately due to being fixed in the body by food. The emesis, eructation like troubles do not develop. So, it can be used in weak persons.^[27]

Madhyabhakta (In the middle of the meal) - It is useful in diseases caused by *Samaana Vata*, in diseases of the *Koshta* and diseases of *Pitta* origin. *Chakrapani* and *Indu* states that half of the food is taken first then followed by the intake of *Aushadha* then the remaining half of food. The medicine taken in middle of meals getting obstructed in both the ways by diet extracts the *Doshas* situated in internal organs very easily.^[28] It is desired in mild diseases.^[29]

Adhobhakta (After the meal drug is taken) - *Hemadri* and *Indu* states that *Bheshaja* is to be administered immediately after meals. In diseases due to *Vyanavata*, it should be after the morning meal and in diseases due to *Udanavata* it should be after the

evening meal. This method is useful for strengthening the upper part of the body, cure of their diseases and for diseases caused by *Kapha*, to cause stoutness of the body.

Sabhakta (Mixing the drug with the food during preparation, after preparation or eating immediately after the drug administration) - This type of *Kaala* indicated for children, persons who are of tender constitution, those who hate medicines, in loss of appetite and diseases affecting the whole body.

Antara bhakta (intake medicine in midday after the digestion of the forenoon meal. Then meal can take at the evening after the digestion of medicine). It is for those who have strong digestion and in disorders caused by *Vyanavata*.

Samudga (Intake of medicine twice, once just before meals and once again immediately after meals). Drug should be having digestive property and be in the form of *Leha* (confection), *Choorna* (powder) are taken in this *Kaala*. It is advised in *Hidma* (hiccup), *Kampa* (tremors), *Aakshepa* (convulsions), and when the *Dosas* are localized at both upper and lower parts of the body. *Antara Bhaktam Kaala* is also same as *Samudga*. It is advised to take the medicine in event of *Doshas* having gone upward and downward, in opposite way (before and after meals).^[30]

Muhurmuhu (Use frequently with or without food) - In *Swasa* (dyspnoea), *Kasa* (cough), *Hidma* (hiccup), *Trut* (thirst), *Chardi* (vomiting), and in *Vishavikara* (diseases caused by poisons).

Sagrasa (Only once with morsel of food). In this *Kaala* drugs should be in the form of *Choorna* (powder), *Leha* (confection), *Vataka* (granules) and having the *Agni-deepana* (digestive fire stimulating) property. It is advised in *Prana Vata* disorders, and *Vajeekarana* (aphrodisiacs) medicines are used as *Sagrasa*.

Grasantara (After every morsel)- In *Prana Vata* disorders. Drugs which cure diseases like *Hrudroga* (disease related to heart), Drugs to produce vomiting,

Dhoomapanadravyas (smoking drugs) are advised to take in this *Kaala*.

Nisi (Bed time) - In *Jatrurdharogas* (diseases above the shoulder). This time is ideal for *Lekhana* (cureting), *Brimhana* (strengthening and nourishing), *Pachana* (digestive action) and *Shamana* (palliative action) purpose.^[31] Medicines should be given on empty stomach at night. In *Deepika* commentary it is mentioned that the timing of administration of medicine is 1 *Yaama* (3hr) after evening meals.

References from classics for the intake of medicine according to *Bheshaja Kaala* are listed in Table number 3.

Table: 3 References from classics for *Bheshaja Kaala*

Adhikarana	Yogam	Reference
<i>Prameha-Pratah Niranna</i>	<i>Haridra+Madhu+Amalakiswarasa</i>	A.S.Ci14/5
<i>Vishamajwara-Pragbhakta</i>	<i>Kalyanaka Ghrita,Shatpalaghrita</i>	A.H.Ci 1/154
<i>Grahani-Madhya Bakta</i>	<i>Yavagu+Ghrita</i>	A.H.Ci10/75
<i>Rajyakshma-Adhobakta</i>	<i>Rasnaghritam</i>	Ch.Ci 8/94
<i>Gulmam- Sagrasa</i>	<i>Ashtachooram+Ghrita</i>	A.H.Chi14/35
<i>Udara-Muhurmuhu</i>	<i>Ghrita Prayogam</i>	A.H.Ci 15/36
<i>Arshorogaadhikar a-Samudga</i>	<i>Praanada Gutika</i>	B.R/58-59
<i>Netra Balyam-Nishi</i>	<i>Triphala+Madhu+Sarpi</i>	A.S.Su10

Likewise, the *Triphala Modaka* is given before the meal in between the meal and after the meal in diseases of lower extremities, abdomen and head & neck respectively.^[32] This also shows the endogenous effect of circadian rhythm. Moreover, it has been also described that the diseases occurring due to effect of time should be treated even before the onset of

symptoms of diseases. Not only the drugs but the food articles given at different times also have different effect like: intake of milk at morning is *Balya* (strengthening), *Brimhana* (nourishing) and *Agni vardaka* (appetizing). If it is in noon, it enhances *Bala* (strength), cures *Mootrakrucha* (dysuria) and *Asmari* (stones). The same taken at night become pacifier for many disorders.^[33] Similarly sugarcane if taken before meal alleviates *Pitta* while taken after meal aggravates *Pitta* and in between meals delays its digestion.^[34] Effect of *Jala Pana* (water intake) with respect the *Annakala* (food intake time) also shows difference like *Jala* at *Bhukthadau Kaala* (before meals) it causes weakness of the digestion and emaciation of the body. In *Bhukthamadhya Kaala* (in between meals) it maintains the normalcy of the tissues and helps for easy digestion. And at the end of the meals, it cause obesity and accumulation of *Kapha* in the parts above the stomach.^[35]

DISCUSSION

For the proper metabolism of *Aushadha* and *Ahara* proper *Agni* should be there. Drug metabolism is one among the pharmacokinetics processes. As per *Ayurveda* in *Abhakta Kaala Agni* and *Aushadha* interaction is unobstructed because of absence of food and *Agni* will be in *Pradeeptha* Avastha. *Hemadri* clarifies that medicine should be administered in the *Kapha Udreka Gata Kaala*.^[36] In *Kapha Kaala*, *Agni* (digestive fire) will be in *Mandavastha* (less powerful state). *Kapha Kaala* is one-third part of the day, and later half of this one-third part is *Kapha Udreka Gata Kaala*. As per *Indu Bheshaja* should be given 3 hours after sunrise in *Abhakta kaala*.^[37] This shows the importance of time for the administration of drug. *Praagbhakta* is administration of the drug just prior to the meal. Thus, it is the first target of *Agni* and not the food. In this *Kaala* the *Bheshaja* digests immediately. This *Kaala* is advised mainly for *Apana Vata* vitiation. So, in case of *Mootravaha*, *Malavaha*, *Shukravaha Srotovikara*, *Arsas* (hemorrhoids), *Gudabramsha* (rectal prolapse) this type of *Kaala* can be adopted. *Madhyabhakta* is administration of the drug in the middle of the meal. So, the medicine can't spread and is forced to act locally and eradicate the *Sthanika*

Doshas. As *Samana Vayu* and *Pachaka Pitta* are in *Koshta* this type of *Kaala* helps to control the *Paithika* and *Koshtagata Vyadis*. *Adhobhakta* is use of the drug after the meal. In *Vyana Vikruti* the drug administered after the lunch and in *Udana Vikruti* after dinner can stimulate these *Vata* and can corrects its dysfunctions. By the action of *Udanavayu*, the *Urdhvagati* of *Bheshaja* becomes easier, there by strengthening the upper parts of body. In this prolonged effect of *Agni*, *Bheshaja* interaction is expected. pH of the stomach is one dependent factor for the action of *Bheshaja*. It might be one of the reasons behind before and after administration of food. According to *Indu Sabhakta* is partaking food prepared by mixing the drug like some *Yavagu* (porridge) preparations or mixing the drug to the prepared food and eating immediately. The expected activity of *Bheshaja* in this type is to potentiate the *Agnibala* and the drug mixes with *Rasa Dhatu* and spread all over the body through *Urdhva*, *Adha* and *Tiryakgati*. So, this type of *Kaala* can be used in *Sarvanga samsrita vyadhis*. In this type of *Kaala* and in *Grasa Kaala* maximum availability of the *rasa* of the *Bheshaja* is expected. According to *Ayurveda* mainly two *Annakala* is described.^[38] So in *Antarabhakta Kaala* (in between food), after the digestion of morning meal the drug is administered in midday so in this *Madyahna* (midday) the *Agni* (digestive fire) is in stimulated condition and after the drug metabolism again food is taken in evening. This type can be given in the night also. In this type of *Kaala*, *Agni* (digestive fire) and *Bheshaja* interaction occurs. It is mainly used in *Vyana Vatajanya Vikaras*. Vitiating of *Vyana Vata* hampers its functions as well as nutrition and movements of the body. It can circulate the whole body. The main site of *Vyana* is *Hridaya* (heart). *Ayurveda* explains the functions of *Hridaya* (heart) in relation to sun-moon cycle. *Samudga* provides the localized action of the *Bheshaja* on *Anna*. The medicines which having the *Utklesha Kara* property, which cause *Glani* (languor) like *Vikaras* should not be used in this *Kaala*. It promotes *Urdhva* (upward) and *Adhogati* (downward movement) of the drug and helps in correcting *Gati Vikruti* (disturbance in normal movement) of *Vata Dosh* by promoting *Anulomana*

(downward movement) of *Vata dosha*, eg: in *Hikka* (hiccup) both *Vata* and *Kapha dosha* are involved.^[39] The *Sthana* (site) of *Kapha* is *Urdhwashareera* (upper part of body) and of *Vata* is *Adhashareera* (lower part of the body). *Bheshaja* (medicine) administered in this *Kaala* can pacify both the *Doshas* in both parts of the body. *Muhurmuhu* is the use of medicine, frequently with or without food. In this type prolonged effect of *Agni-Bheshaja* interaction is expected and treats the vitiated *Doshas* in their *Sanchaya* and *Vegavastha* and the blood level concentration of medicines is to be maintained at par round the clock. This is adopted in conditions where *Pranavaha Srotodushti*, *Udakavaha Srotodushti*, *Annavaha Srotodushti Vikaras* occurs. In repeated administration, accumulation of drug occurs when it is administered before the previous dose is completely eliminated. Then the amount of drug in the body progressively increases. When the rate of drug elimination compensates the rate of drug administration, the average drug concentration reaches steady state. *Sagrasa* is taking medicine only once with morsel of food so that it facilitates absorption of drug from buccal mucosa. *Grasaantara* is taking it after every morsel and having the property of kindling digestion. According to *Arunadatta* and *Hemadri* in this *Kaala*, *Bheshaja* is mixed with every morsel of food. So, the concentration of medicine will be more and causes the faster actions in this *Kaala*. Both this *Kaala* used in *Prana Vayu Vikaras*. Normally *Prana Vayu* regulates the intake of food,^[40] so medicine with *Grasa* can stimulate the *Prana Vayu* thereby it can cure the *Prana Vayu* vitiated diseases. The factors which influence drug administration in relation to food, including pharmacokinetics, efficacy and, improving patient tolerance by minimizing gastrointestinal upset.^[41] *Nisi Kaala* provides prolonged time activity of the drug as in *Nisi Kaala* all the metabolic activities are slowed down compared to the day. One of the factors for drug administration depends on the state of the CNS. That might be the reason behind the medicines at night for disease above the shoulders, when CNS is relatively at rest. The time of drug administration depend up on so many factors. These include the cyclic variation of *Doshas* and the rate of metabolism of drugs depends

on *Agni Bala* of the patient and presence or absence of food. *Mahaveerya Bhesaja* (medicines having strong potency) possess a strong energy level of action and it can stimulate the *Agni* at bits gross levels. This indicates the pharmacodynamic action of the *Bhesaja*. While discussing about the *Bhesajakaala*, *Vatadosha* is taken in to account. Etymological derivation of the term *Vata* is *Gati, Gandhana*^[42] means to initiate, to excite and to stimulate. *Vata Dosha* controls all functions of body. *Agni* present in the *Jathara* which digests the food is served by *Prana, Apana* and *Samana* by blowing/increasing, protecting and preserving it helps other *Agni* to carry on their respective functions properly and which is controlled by the appropriate *Aushadha Kaala*. One can apply *Aushadha Kaala* to *Pitta* and *Kapha* according to *Sthana Samanya* of *Dosas* as which is described in table 4.

Table 4: Sthana Sadharmya of Doshas

Vata Prakara	Sthana Sadharmya
Prana Vata	Avalambaka Kapha
Udana Vata	Avalambaka Kapha
Vyana Vata	Sadhaka Pitta
Samana Vata	Pachaka Pitta Ranchaka Pitta Kledaka Kapha
Apana Vata	-

CONCLUSION

The treatment of the curable disease is done after ascertaining the diseases on the basis of clinical features of *Doshas* by prescribing the therapies contrary to etiological factors and also giving due consideration to *Matra* (dose) and *Kaala* (time of administration).^[43] The success of *Chikitsa* depends upon proper planning for use of drugs about their quantity and *Kaala* of administration. Hence, knower of proper planning of administration stands at a higher place than knower of drug.^[44] Evaluation of *Shadaveksha Kaala* plays an important role in deciding

Bhaishajya. The ultimate goal of attaining the *Dosha, Dhātu Samyata* can very well be done by suggesting a proper *Aushadha Sevana Kaala*. *Vata Dosha* is given prime importance in the context of *Aushadha Sevana Kaala* and there is much importance for *Agnibala* of the patient also. It is meant for *Shamana Chikitsa* only. The effectiveness of many drugs in many diseases varies depending on the time of administration in associated with 24 hours biological rhythm under the control of circadian clock. *Aushadha Sevana Kaala* is a further dimension for research aiming that safer and efficient disease therapy in future. Treatment done earlier to the proper time or treatment not done at the proper time and treatment being either inadequate or in excess, these do not succeed even in curable diseases.

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