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A REVIEW ON CHRONOBIOLOGICAL PERSPECTIVES ON AUSHADHA SEVANA KALA: INTEGRATING AYURVEDIC THERAPEUTIC TIMING WITH MODERN CHRONOTHERAPY

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ABSTRACT

Aushadha Sevana Kala constitutes a fundamental principle of Ayurvedic therapeutics, underscoring the importance of medication timing in determining therapeutic efficacy alongside the pharmacological properties of the medicinal agent. In Ayurveda, therapeutic efficacy depends not only on the drug administered but also on the temporal and physiological context of its administration, including before meals, after meals, at night, or at specific intervals relative to food intake. Classical Ayurvedic texts, including Charaka Samhita, Sushruta Samhita, Ashtanga Sangraha, Ashtanga Hridaya, Kashyapa Samhita, and Sharangadhara Samhita, describe Aushadha Sevana Kala, although its nomenclature, number of timings, and specific therapeutic applications vary. This review critically examines the major Aushadha Sevana Kala and explores their conceptual significance and therapeutic rationale. It also correlates these classical concepts with contemporary understanding of gastrointestinal physiology, motility, drug absorption, and pharmacokinetics. Modern chronotherapy similarly emphasizes that endogenous biological rhythms can influence drug absorption, distribution, metabolism, and therapeutic response, indicating that the timing of drug administration may significantly affect treatment outcomes. From this perspective, Aushadha Sevana Kala and chronotherapy reflect a shared principle of time-dependent therapeutic response, though their conceptual frameworks differ: Ayurveda emphasises Agni, Dosha, and Bala, while modern pharmacology focuses on physiological and pharmacokinetic mechanisms. A distinctive feature of the Ayurvedic approach is its individualised consideration of therapeutic timing. Rather than relying solely on chronological time, Ayurveda considers factors such as digestive capacity, individual constitution, and disease characteristics when determining the appropriate time for medication administration.

Keywords: Aushadha Sevana Kala, Chronotherapy, Integrating Medicine

INTRODUCTION

Ayurveda, a time-tested framework of health and harmony, rests on the fundamental principles of Hetu (causative factors), Linga (clinical manifestations), and Aushadha (therapeutic measures), collectively known as the Trisutra [1]. These three pillars provide a systematic approach to understanding disease: identifying its cause, recognising its manifestations, and culminating in appropriate treatment. Among them, Aushadha represents the practical application of Ayurvedic knowledge, aimed not merely at alleviating symptoms but at restoring Dosha equilibrium and maintaining health.

Ayurvedic therapeutics extends beyond selecting an appropriate medicine. The classics emphasise that treatment efficacy depends on several factors, including the nature of the drug, the patient, the disease, dosage, and, importantly, the time of administration. This concept, known as Aushadha Sevana Kala, is a distinctive feature of Ayurvedic pharmaco-therapeutics. The term Aushadha Sevana Kala is derived from three words: Aushadha, meaning medicine; Sevana, meaning administration or intake; and Kala, meaning the appropriate time. Thus, Aushadha Sevana Kala refers to the prescribed time for administering medicine. It advocates administering medicines at specific times relative to food intake, digestion, and the body's physiological state to maximise therapeutic benefit.

A medicine's therapeutic efficacy depends not only on what is administered, but also on when it is administered. Modern chronopharmacology has shown that drug timing significantly influences absorption, distribution, metabolism, therapeutic response, and adverse effects. Remarkably, centuries before chronotherapy emerged, Ayurveda emphasised Aushadha Sevana Kaala, the appropriate timing of medicine administration based on the individual's physiological state, meal timing, and disease condition. The right medicine given at the wrong time may not produce the desired therapeutic effect.

Ashtanga Sangraha emphasises the significance of Kala in drug administration by stating, "Kalo Bhaisajya Yogakṛit", implying that the appropriate timing of medicine administration is essential for achieving the desired therapeutic effect of Aushadha. [2]

Acharya Hemadri calls this concept Shamanoushadha Kala, indicating that these drug-administration timings apply to Shamana Chikitsa and not to Shodhana Chikitsa [3]. Furthermore, the concept primarily pertains to orally administered medications, as they first interact with Agni, which plays a crucial role in their digestion, metabolism, and therapeutic action.

Bhaishajya Kaala, Aushadha Sevana Kaala, Bhaishajya Grahana Kaala, Aushadha Avacharana Kaala, Agada Kaala, and Aushadha Vekshana Kaala are synonyms for the time of drug administration.

Table 1: Number of Aushadha Sevana kala according to different acharyas

Charaka Samhitha	10
Susruta Samhitha	10
Astanga Hridaya	10
Astanga Sangraha	11
Sarngadhara Samhitha	5

Table 2: Summarising the Aushadha Sevana Kala mentioned in classics

Ch.Chi.30	Su.Ut. 64	A.S.Su.23	AH.Su.13	Ka.Khi.3	Sh.Pu.2
Pratareva niranna	Abhakta	Abhaktha	Ananna	Abhaktha	Prabhathe
Bhukthadou	Pragbhaktha	Pragbhaktha	Annadou	Purva bhaktasya	Divasa bhojane
Bhuktha madye	Adhobhaktha	Madhye bhaktha	Madhye bhaktha	Madhye bhaktha	Sayanjate bhojana
Pratah bhaktapashchat	Madhyebhaktha	Madhyabhaktha	Bhojanante	Adhobhaktha	Muhurmuhu
Sayam bhaktapashchat	Antarabhaktha	Antarabhaktha	Kabalantare	Bhakthayo madhye	Nishi
Muhurmuhu	Sabhaktha	Sabhaktha	Muhurmuhu	Muhurmuhu	
Samudga	Samudga	Samudga	Samudga	Saamudga	
Bhakthasamyuktha	Muhurmuhu	Muhurmuhu	Saannam	Sabhaktha	
Grase	Sagrasa	Graaasa	Grasa	Graasa	
Grasantare	Grasantara	Grasantara	Nisi	Graasantara	
		Nisi			

ABHAKTHA

According to Ashtanga Sangraha, medicine should be administered in the morning after the aggravated Kapha has cleared from the stomach[2]. Acharya Chakrapani interprets Abhaktha as the administration of medicine in the morning only after the previous meal has been completely digested[1]. Indu recommends administering medicine one Yama (approximately three hours) after sunrise [4], whereas Hemadri advises its administration during the period of Kapha Udreka Gata Kala, after the phase of increased Kapha has subsided.[5]

According to Susrutha during administration of Aushadha in this Kala there will be Heena Avastha of anna and veeryaadhikya of Aushadha so that disease gets cured easily.

Indications: Lekhanartha, Utklishtakapha Pitta, Kaphaudreka Kaal, Prabala Vyadhi in Balavan Purusha.

Contraindications: Bala, vrudha, and stree may not tolerate the potency of medicines administered on an empty stomach. In such individuals, administration of drugs in the fasting state may lead to complications such as glani (fatigue) and bala-kṣaya (loss of strength).

Administration of medicines in the morning on an empty stomach offers several physiological advantages that enhance their therapeutic efficacy. In the fasting state, the stomach is relatively empty, allowing rapid gastric emptying and quicker delivery of the drug to the small intestine, the primary site of absorption because of its large surface area, abundant villi and microvilli, and rich blood supply.[6] During this period, the interdigestive migrating motor complex (MMC), a cyclic pattern of gastrointestinal motility occurring every 90–120 minutes between meals, acts as an "intestinal housekeeper" by clearing residual food particles, mucus, cellular debris, and bacteria from the stomach and small intestine. This cleansing action minimises interference with orally administered drugs and promotes rapid transit to the small intestine's absorptive surface, enhancing drug absorption and bioavailability. Furthermore, the absence of food prevents food–drug interactions that can delay gastric emptying, alter gastric pH, increase gastric viscosity, or form drug complexes, resulting in more consistent absorption, a faster onset of action, and more predictable plasma drug concentrations.

Additionally, morning administration aligns with the body's circadian rhythm, as gastrointestinal motility, intestinal blood flow, and endogenous cortisol levels begin to increase after awakening, potentially optimising drug absorption and therapeutic response.

PRAGBHAKTHA

Pragbhakta refers to administering medicine immediately before food. Acharya Charaka recommends this timing for disorders of Apana Vata [7]. According to Acharya Sushruta, medicines administered before meals undergo sheeghra vipaka and do not cause loss of strength; because food covers them, they are retained in the body and not expelled [8]. Ashtanga Sangraha states that this mode of administration strengthens adha kaya [2]. While Kashyapa Samhita mentions that it helps eliminate amashayayagata doṣas [9]. Sharangadhara mentions it as a subdivision of Divasa Bhojana Kala.[10]

Administering medicines immediately before food allows drug absorption to begin during fasting, enabling therapeutic plasma concentrations at the onset of meal ingestion. This temporal synchronisation aligns the drug's pharmacological action with the physiological transition from the interdigestive to the postprandial state. Meal intake activates integrated neurohormonal mechanisms, including vagal stimulation, enteric nervous system activation, and the secretion of gastrointestinal hormones such as gastrin and cholecystokinin, which collectively coordinate gastric emptying, antral contractility, intestinal peristalsis, and the gastrocolic reflex [6].

Consequently, gastrointestinal motility shifts from the interdigestive migrating motor complex to the fed motility pattern, characterised by coordinated propulsive contractions that facilitate the aboral movement of luminal contents. Medicines administered immediately before meals are therefore pharmacologically active during this critical phase of gastrointestinal motor activity, enabling them to modulate smooth muscle contractility, enhance coordinated peristaltic activity, optimise gastrointestinal transit, and improve the efficiency of propulsive motor function.

MADHYAMABHAKTHA

Madhyabhakta means administration of Aushadha in between meal. According to Acharya Chakrapani, half of the meal should be consumed initially, followed by the administration of the medicine, after which the remaining half of the food is taken [7]. Acharya Sushruta explains that, because of the medicine's Avisaari Bhava (non-diffusive nature), it primarily exerts its therapeutic action on diseases affecting the Madhya Deha [11]. Similarly, Acharya Kashyapa states that, being enclosed by food (Avarodha), the medicine acts predominantly on disorders of the Antarashaya [9]. Acharya Sharangadhara also describes this mode of drug administration as a subdivision of Divasa Bhojana Kala.[10]

Administering medicines during a meal allows the drug to act when digestive activity is at its peak. The initial portion of food activates the cephalic and gastric phases of digestion through vagal stimulation, leading to the secretion of gastric acid, digestive enzymes, bile, and gastrointestinal hormones such as gastrin and cholecystokinin. At the same time, gastrointestinal motility shifts from the interdigestive migrating motor complex to the fed motility pattern, characterised by coordinated mixing contractions and peristalsis. These neurohormonal and motor responses create an optimal environment for drug disintegration, dissolution, and interaction with the gastrointestinal mucosa. Subsequent food intake promotes uniform mixing of the drug with chyme, prolongs gastric residence when appropriate, facilitates gradual delivery to the small intestine, minimises gastric irritation, and reduces gastroesophageal reflux.

ADHOBHAKTHA

Aushadha is administered after the food. Acharya Chakrapani states that this Kaala is divided into Praatar Bhojanottara Kaala (after the morning meal) and Saayam Bhojanottara Kaala (after the evening meal [7]. According to Acharya Sushruta, administration of medicine at this time promotes Bala [11]. Ashtanga Sangraha mentions that it alleviates Kapha and promotes nourishment [2]. Acharya Sharangadhara describes it as Bhojanaante under Divasa Bhojana, and also recommends Saayam Bhojanaanta Kaala under Saayam Bhojana for the management of Prana Vata disorders.[10]

Administering medicines after food uses the postprandial physiological state to improve drug tolerability and therapeutic efficacy. Food stimulates mucus and bicarbonate secretion, protecting the gastric mucosa and reducing gastrointestinal irritation. Postprandial hyperemia increases splanchnic blood flow, while delayed gastric emptying promotes gradual drug absorption, reducing abrupt fluctuations in plasma drug concentrations and enhancing cardiovascular stability. Additionally, a meal, particularly one containing dietary fat, stimulates CCK release, leading to gallbladder contraction and bile secretion. Bile salts facilitate micelle formation, thereby enhancing the solubilization and intestinal absorption of lipophilic drugs.

ANTARABHAKTA

Antarbhakta Kaala refers to administering Aushadha between two meals. Bhaktayor Madhye and Antarbhakta are considered synonymous terms for this period. According to Ashtanga Sangraha, the medicine is administered after the afternoon meal is fully digested, and the next meal is taken only after the medicine has been adequately digested. Acharya Jejjata, in his commentary on Charaka Samhita, describes this period under Madhyabhakta Kaala. According to Indu, Antarbhakta Kaala includes two periods: the first occurs during the daytime, while the second is approximately one Yaama (three hours) after the evening meal, corresponding to Nishi Kaala. This mode of drug administration is also described in Sushruta Samhita, Ashtanga Sangraha, and Kashyapa Samhita. Indications are Antarbhakta Kala is indicated for drugs intended to promote cardiac well-being (Hṛdya), mental strength (Manobalakara), enhancement of digestive power (Dipana), and in conditions involving vitiation of Vyana Vayu.

Administering medicines between meals, when the stomach is relatively empty, minimises food–drug interactions and interference from dietary components such as calcium, iron, and dietary fibre, improving the rate and consistency of drug absorption. In the absence of food, gastric emptying is generally faster, allowing the drug to reach the small intestine—the principal site of absorption—more rapidly, resulting in an earlier onset of action and, for many drugs, improved bioavailability. Reduced competition with nutrients for intestinal transport mechanisms and decreased dilution by gastric contents contribute to more predictable pharmacokinetics and consistent therapeutic plasma concentrations. This timing also allows digestive stimulant drugs to interact directly with the gastrointestinal mucosa, enhancing gastric and pancreatic secretions and improving digestive function. Additionally, more predictable systemic absorption facilitates efficient distribution of the drug to target tissues via the circulation. Between meals, postprandial increases in splanchnic blood flow have subsided, resulting in more stable systemic hemodynamics and potentially more predictable systemic drug distribution.

SAMABHAKTHA

Sabhakta Kala refers to administering Aushadha with food, either during cooking or by mixing it into the prepared meal. Bhakta Samyukta and Sanna are synonymous terms. According to Kashyapa, this Kala helps maintain Bala and Agni, while Sharangadhara describes it under Divasa Bhojana. Vyana Vayu distributes the medicine throughout the body through Rasa. Indications are Aruchi, Mandagni, and in children, elderly women, Kṣata-kṣiṇa, Sukumara, and Sarvangagata Roga.

Mixing medicines with food improves palatability by masking unpleasant tastes, odours, and textures, making them more acceptable to the patient. Pleasant taste stimulates the taste buds on the tongue, activating gustatory receptors and increasing salivary secretion through parasympathetic reflexes.[6] Enhanced salivation lubricates the oral cavity, facilitates swallowing, initiates carbohydrate digestion, and promotes the cephalic phase of digestion by stimulating gastric acid and digestive enzyme secretion. This physiological response prepares the gastrointestinal tract for efficient digestion and may improve the dissolution and subsequent absorption of the administered medicine.

SAMUDGA

Samudga Kala refers to administering Aushadha immediately before and after food, with the medicine given in relation to the meal, resembling a Samputa (enclosure). According to Ashtanga Sangraha, Avaleha, Navana, and Pana are suitable forms of medication for this Kala. It is considered useful for mitigating Doshas spreading in both upward and downward directions. Sharangadhara Samhita describes it under Divasa Bhojana, while Dalhana, Indu, and Hemadri emphasise administering the medicine immediately with food, preferably in liquid form. Indications are Akshepaka, Hikka, Kampa, and Pravisruta Dosha, particularly disorders involving Urdhva and Adhogata Dosha.

Administering medicine immediately before and after food sustains drug exposure by distributing the dose across the preprandial and postprandial phases of gastrointestinal physiology. The presence of food delays gastric emptying through the release of cholecystokinin (CCK) and other enterogastrones, prolonging gastric residence time and promoting gradual delivery of the drug to the small intestine [6]. This controlled transit can result in more sustained absorption and prolonged maintenance of therapeutic plasma concentrations. Divided dosing around meals reduces peak–trough fluctuations in plasma drug levels, thereby producing more stable pharmacokinetic profiles and minimising variations in pharmacodynamic response.

MUHU MUHU

Muhurmuhu Kala refers to the repeated, frequent administration of Aushadha, with or without food. According to Charaka and Sharangadhara, the medicine is administered repeatedly during meals, whereas Susruta and other Acharyas recommend frequent administration irrespective of meals. It is classified into Abhakta Muhurmuhu and Sabhakta Muhurmuhu, selected according to the patient's Bala [12].

This Kala is particularly useful in conditions with continuous or recurrent symptoms, ensuring a sustained therapeutic effect. Indications are Hikka, Swasa, Kasa, Chardi, Tṛṣṇa, Viṣa, Garaviṣa, and Svarabhanga.

Repeated administration of medicine at short intervals helps maintain therapeutic drug concentrations by compensating for ongoing drug elimination through metabolism and excretion. Frequent dosing minimizes fluctuations between peak and through plasma concentrations, ensuring sustained receptor occupancy and a more consistent pharmacological response. This dosing strategy is particularly beneficial in conditions characterised by continuous or recurrent symptom episodes, where uninterrupted therapeutic activity is required. Maintaining relatively stable plasma concentrations also reduces the risk of breakthrough symptoms that may occur when drug levels fall below the minimum effective concentration. Thus, repeated dosing supports continuous pharmacodynamic effects throughout the period of persistent symptom activity.

SAGRASA

Grasa Kala denotes administering Aushadha with every morsel of food. Grase-Grase and Sagrasa are alternative terms for this Kala. It is particularly appropriate for medicines in the form of Churṇa, Vaṭi, and Leha. Churṇa administered in this manner may enhance Agni, possibly due to its Rukṣa property, while administration with each morsel may promote buccal absorption and support the function of Praṇa Vayu. [13] Indications are Agni Dipana, Praṇa Vayu Duṣṭi, Vajikaraṇa, and conditions associated with Kṣiṇa and Alpasukra.

Administration of medicine along with each morsel of food provides repeated stimulation of gustatory receptors during mastication, activating parasympathetic pathways through the cephalic phase of digestion. This neural stimulation enhances salivary secretion and promotes vagally mediated secretion of gastric acid, pepsin, pancreatic enzymes, and bile, thereby facilitating efficient digestion. Continuously mixing the medicine with successive food boluses ensures prolonged contact with the oral cavity and gastrointestinal mucosa, sustaining stimulation of digestive secretions throughout the meal. In addition, thorough mastication and repeated oral sensory stimulation improve bolus formation and gastrointestinal preparatory responses, thereby enhancing overall digestive efficiency and supporting optimal nutrient digestion and absorption.

NISHI

Nishi Kala refers to administering Aushadha at night, particularly at bedtime. Swapna Kala and Ratri are synonymous terms. According to the Dipika commentary on the Sharangadhara Samhita, the medicine is administered about one Yama (three hours) after the evening meal. This method is described in Ashtanga Sangraha, Ashtanga Hridaya, and Sharangadhara Samhita. Indicated Mainly in Urdhvajatru Vikara and for Lekhana and Brimhana therapies targeting disorders of the Urdhvajatru region.

Bedtime administration prolongs contact time of locally acting formulations with the oral cavity, pharynx, and upper respiratory mucosa because swallowing frequency, speech, and oral intake are markedly reduced during sleep. This extended mucosal residence time may enhance local drug retention, improve mucosal absorption where applicable, and prolong therapeutic action. Overnight fasting minimises dilution and clearance by food and beverages, while reduced mechanical removal from swallowing and mastication allows sustained exposure of affected tissues to the medication.

CHRONOTHERAPY AND ITS CONCEPTUAL RELATIONSHIP WITH AUSHADHA SEVANA KALA

Chronotherapy is a therapeutic approach that times the administration of medicines or other interventions to the body's biological rhythms to optimise efficacy and minimise adverse effects. It is based on the idea that physiological functions, disease activity, drug absorption, metabolism, distribution, and elimination may vary over the day because of circadian and other biological rhythms. Therefore, administering a drug at an appropriate time can enhance its desired pharmacological effect while reducing toxicity. Chronotherapy thus emphasises that "when a treatment is given" can be as important as "what treatment is given," providing a basis for more individualised and physiologically aligned therapy.

Chronotherapy is a therapeutic approach based on the principle that intervention timing can influence efficacy and safety because physiological functions, disease activity, drug targets, and pharmacokinetic processes follow predictable biological rhythms. It broadly encompasses two major concepts: "clocks as targets" and "clocks as modulators" [14].

In the former, interventions such as light exposure, time-restricted feeding, appropriately timed exercise, and pharmacological modulation of clock-related pathways modify or synchronise circadian rhythms.

In the latter, endogenous biological rhythms help determine the most appropriate timing of drug administration. Circadian variations in drug-target expression, absorption, distribution, metabolism, excretion, and disease activity may influence therapeutic response; therefore, appropriately timed medication can potentially maximise efficacy and minimise adverse effects.

A comparable time-oriented therapeutic principle appears in the Ayurvedic concept of Aushadha Sevana Kala, which prescribes administering Aushadha at specific times relative to food intake, digestion, day–night cycles, and the physiological predominance of Dosha and Vayu. Ayurveda selects various Sevana Kala, such as Abhakta, Pragbhakta, Madhyabhakta, Antarbhakta, Sabhakta, Samudga, Muhurmuhu, Grasa, and Nishi, based on the nature of

the disease, the patient's strength, digestive capacity (Agni), and the intended therapeutic action.

Thus, while chronotherapy explains time-dependent treatment through circadian biology and temporal variations in physiology and pharmacology, Aushadha Sevana Kala offers an individualised Ayurvedic framework for optimising drug administration based on the patient's physiological state and disease characteristics [15].

Therefore, both concepts share a fundamental principle: the therapeutic outcome may depend not only on what medicine is administered, but also on when and under what physiological conditions it is administered. This conceptual similarity offers a potential integrative framework for exploring Aushadha Sevana Kala through modern chronobiology and chronotherapy, while recognising that Ayurvedic and modern frameworks rest on distinct theoretical foundations.

DISCUSSION

The concept of Aushadha Sevana Kala reflects a level of clinical sophistication in classical Ayurveda that goes well beyond simply choosing "what" medicine to give. The consistency across independently authored texts, despite differences in terminology, suggests that Aushadha Sevana Kala was not an incidental observation but a deliberately developed clinical principle refined through repeated practice and observation. When each Kala is examined individually, a clear physiological logic emerges that aligns well with modern gastrointestinal science. Taken together, these Kalas show that Ayurveda was, in effect, practising an early and intuitive form of pharmacokinetic reasoning, long before the biochemical mechanisms behind gastric emptying, motility, and absorption were understood in molecular detail.

What is particularly noteworthy is how this classical framework compares to modern chronotherapy. Chronotherapy is grounded in circadian biology: the idea that drug targets, metabolic enzymes, and disease activity fluctuate across the 24-hour cycle, and that aligning drug administration with these rhythms can improve efficacy and reduce toxicity.

Aushadha Sevana Kala reaches a similar conclusion through a different lens, factoring in Agni, Dosha, Bala, and the nature of the disease rather than circadian gene expression or hormonal cycles. Despite this difference in theoretical grounding, both systems converge on the same practical insight: treatment effects cannot be separated from the timing of administration. This convergence matters because it suggests that Ayurvedic dosing schedules, rather than being purely traditional or empirical, may have an underlying physiological rationale that modern pharmacology is only beginning to document formally.

That said, several limitations must be acknowledged. Much of the physiological reasoning connecting Aushadha Sevana Kala to modern chronopharmacology in this review is interpretive and conceptual rather than experimentally validated.

Few clinical or pharmacokinetic studies directly test whether administering Ayurvedic formulations at the classically prescribed times produces measurably different therapeutic outcomes than other timings. Additionally, terminology and classification of these Kalas differ across texts, creating ambiguity when translating classical instructions into standardised modern protocols. Bridging this gap would require targeted pharmacokinetic and pharmacodynamic studies on specific Ayurvedic formulations administered at their designated Kalas, ideally with objective measures of absorption, bioavailability, and clinical response.

CONCLUSION

Timing matters just as much as the medicine itself; that's the core message of Aushadha Sevana Kala. Ayurveda worked this out centuries ago, laying down clear instructions on when to take a medicine in relation to food, digestion, and the body's natural state.

What's remarkable is that modern science, through chronotherapy and pharmacokinetics, is now reaching the same conclusion: the body's rhythms genuinely affect how well a drug is absorbed and how well it works. The language differs Ayurveda speaks of Agni, Dosha, and Bala, while modern medicine speaks of gut motility and drug metabolism, but the underlying insight is the same. This overlap isn't just a curiosity; it points to a real opportunity to study Ayurvedic dosing timing more rigorously and bring these two systems of knowledge closer together.

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