

# Chronotoxicology and Tridoṣa How Circadian Rhythms Influence Viṣa Vega

Dr. Sankalan Bhattacharya<sup>1</sup>, Dr. Sasanka Shekhar Choudhury<sup>2</sup>

<sup>1</sup>Post Graduate Scholar, Department of Agada Tantra evum Vidhi Vaidyaka, Uttaranchal Ayurvedic College and Hospital, Dehradun, Uttarakhand, India

<sup>2</sup>Post Graduate Scholar, Department of Kriya Shareera, Alvas Ayurveda Medical College and Hospital, Vidyagiri, Moodubidire, D.K, Karnataka, India

## Abstract:

Chronobiology has emerged as an important field explaining the physiological and pathological significance of biological rhythms in human health. Chronotoxicology, a branch of chronobiology, studies the time-dependent variations in toxic responses influenced by circadian rhythms. Contemporary evidence suggests that absorption, distribution, metabolism, detoxification and elimination of toxic substances vary according to biological timing. Ayurveda has long recognized temporal variations in physiology through concepts such as *Dinacharya*, *Ritucharya*, *Doṣa Kāla* and *Vega* dynamics. The present review explored the relationship between chronotoxicology and *Tridoṣa* with special reference to *Viṣa Vega*. Classical Ayurvedic texts describe fluctuations in *Doṣa* predominance across day-night cycles and seasonal transitions, which significantly influence susceptibility, manifestation and progression of toxic conditions. Modern circadian science demonstrates that hepatic enzyme activity, hormonal secretion, gastrointestinal motility, immune responses and neural regulation vary according to circadian oscillations. These mechanisms appear to parallel Ayurvedic descriptions of *Doṣika* dominance and toxic aggravation at specific time periods. This review analysed classical Ayurvedic literature along with contemporary biomedical evidence to understand how circadian rhythms may influence the onset, severity and progression of poisoning. Databases including PubMed, Scopus, Google Scholar and AYUSH Research Portal were searched for relevant literature published between 2000 and 2026. The review highlighted integrative perspectives connecting biological clocks with *Viṣa Vega* progression and emphasized the importance of chronotherapeutic strategies in Ayurvedic toxicology. Understanding temporal biology in poisoning may improve diagnostic accuracy, therapeutic timing and individualized management approaches in integrative medicine.

**Keywords:** Chronobiology, Chronotoxicology, Circadian rhythm, *Tridoṣa*, *Viṣa Vega*, *Agada Tantra*, *Kriya Shareera*

## Introduction

Biological rhythms govern almost every physiological process in the human body. Circadian rhythm, regulated primarily by the suprachiasmatic nucleus of the hypothalamus, synchronizes metabolic, endocrine, neurological and immunological activities according to environmental light-dark cycles. <sup>[1]</sup> Chronotoxicology studies how toxic effects vary depending on the timing of exposure, reflecting the dynamic interaction between biological rhythms and toxic agents. <sup>[2]</sup> Modern toxicological studies have demonstrated significant time-dependent variations in drug toxicity, pesticide metabolism, heavy metal susceptibility and xenobiotic detoxification. <sup>[3]</sup> Hepatic cytochrome

enzyme activity, gastric absorption, renal excretion, cortisol secretion and melatonin release show marked circadian fluctuations, thereby altering toxic responses during different periods of the day. [4]

Ayurveda offers a remarkably sophisticated understanding of temporal physiology through concepts such as *Kāla*, *Dinacharya*, *Ritucharya*, *Doṣa Chaya-Prakopa-Prashama* and *Avasthika Kāla*. [5] The doctrine of *Tridoṣa* explains physiological oscillations occurring in the body according to time, age, diet, environment and seasons. Classical Ayurvedic texts mention that *Vāta*, *Pitta* and *Kapha* dominate specific phases of the day and night, influencing bodily functions and disease manifestations. [6]

*Agada Tantra*, the branch of Ayurveda dealing with toxicology, describes *Viṣa* as a rapidly spreading entity capable of disturbing the equilibrium of *Doṣa*, *Dhātu* and *Mala*. [7] The concept of *Viṣa Vega* refers to the sequential progression and exacerbation of toxic manifestations within the body. [8] Ancient Ayurvedic scholars recognized that timing significantly influences poisoning severity, prognosis and treatment outcomes.

The integration of chronotoxicology with Ayurvedic temporal principles may provide a novel framework for understanding poisoning dynamics. Despite growing interest in circadian medicine, limited scholarly work has explored the relationship between chronobiology and *Viṣa Vega*. Therefore, the present review aimed to critically analyse classical Ayurvedic concepts and correlate them with contemporary chronotoxicological evidence.

## Aims and Objectives

### Aim

To critically review the relationship between chronotoxicology and *Tridoṣa* with special reference to the influence of circadian rhythms on *Viṣa Vega*.

### Objectives

1. To review classical Ayurvedic concepts related to *Kāla*, *Tridoṣa* and *Viṣa Vega*.
2. To analyse modern chrono-toxicological principles associated with circadian biology.
3. To establish possible correlations between circadian rhythm variations and toxic progression.
4. To explore the therapeutic implications of temporal biology in Ayurvedic toxicology.

## Methodology

The present review was conducted using classical Ayurvedic literature and contemporary biomedical databases. Relevant Ayurvedic references were collected from *Charaka Saṃhitā*, *Suśruta Saṃhitā*, *Aṣṭāṅga Hṛdaya*, *Aṣṭāṅga Saṅgraha* and standard commentaries. [5-8]

Electronic databases including PubMed, Scopus, Web of Science, Google Scholar, AYUSH Research Portal and ScienceDirect were searched from January 2000 to March 2026 using keywords such as “chronotoxicology”, “circadian rhythm”, “Ayurveda”, “*Tridosha*”, “*Viṣa Vega*”, “chronobiology”, “biological clock” and “toxicodynamics.” Boolean operators and/or were applied during the search process.

Inclusion criteria involved review articles, experimental studies, clinical studies, toxicological reports and Ayurvedic conceptual analyses discussing circadian physiology and toxic responses. Non-English publications without reliable translation and duplicate studies were excluded.

Data extraction focused on

- Circadian influence on toxicokinetics and toxicodynamics
- Temporal variation in detoxification pathways
- Ayurvedic concepts of *Doṣa Kāla*
- Sequential progression of *Viṣa Vega*

- Chronotherapeutic implications

### Concept of Circadian Rhythm in Modern Science

Circadian rhythms are endogenous biological oscillations with an approximately 24-hour periodicity.<sup>[9]</sup> These rhythms regulate sleep-wake cycles, hormone secretion, metabolism, immunity, cardiovascular function and neurological activities.

The master circadian pacemaker located in the suprachiasmatic nucleus coordinates peripheral clocks distributed throughout various tissues.<sup>[10]</sup> Environmental cues such as light exposure, feeding behaviour, temperature and physical activity synchronize these rhythms.

Major physiological circadian variations include

**Table 1: Major physiological circadian variations**

<i>Physiological Parameter</i>	<i>Peak Timing</i>	<i>Clinical Significance</i>
Cortisol secretion	Early morning	Stress response and metabolism
Melatonin secretion	Night	Sleep induction and antioxidant effect
Gastric acid secretion	Evening/night	Gastrointestinal vulnerability
Hepatic enzyme activity	Variable	Drug metabolism
Immune responsiveness	Night/early morning	Inflammatory regulation

Chronodisruption caused by shift work, irregular sleep patterns, stress or artificial lighting may alter detoxification mechanisms and increase toxic susceptibility.<sup>[11]</sup>

### Chronotoxicology: Concept and Significance

Chronotoxicology studies how biological timing affects toxicity, toxicokinetics and toxicodynamics.<sup>[12]</sup> Experimental evidence demonstrates that the same toxic agent may produce different degrees of toxicity depending upon the time of administration.

Several mechanisms contribute to chrono-toxicological variations

1. Circadian fluctuation in hepatic metabolism
2. Variation in gastrointestinal absorption
3. Altered renal elimination
4. Hormonal modulation of detoxification pathways
5. Immune and inflammatory oscillations
6. Oxidative stress variability

Studies have shown circadian variation in susceptibility<sup>[13]</sup> to

- Heavy metals
- Alcohol toxicity
- Pesticides
- Chemotherapeutic agents
- Snake venom toxicity
- Environmental pollutants

Chrono-toxicological principles are now increasingly used in chronotherapy and precision medicine.

### Ayurvedic Concept of *Tridoṣa* and Biological Timing

Ayurveda recognizes time (*Kāla*) as a fundamental determinant of physiological balance and **Daily *Doṣa* dominance periods.** [5]

Time Period	Dominant <i>Doṣa</i>
6 am – 10 am	<i>Kapha</i>
10 am – 2 pm	<i>Pitta</i>
2 pm – 6 pm	<i>Vāta</i>
6 pm – 10 pm	<i>Kapha</i>
10 pm – 2 am	<i>Pitta</i>
2 am – 6 am	<i>Vāta</i>

**Table 2: Daily *Doṣa* Dominance periods**



**Figure 1: Daily *Doṣa* Dominance periods** [20]

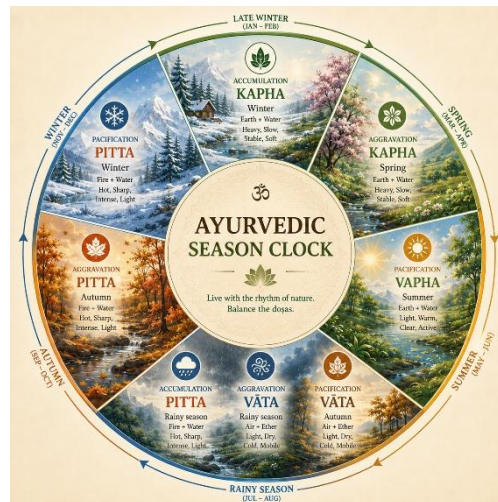
These fluctuations influence digestion, metabolism, cognition, circulation, elimination and mental activity. [6]

Ayurveda also describes **seasonal accumulation** (*Chaya*), **aggravation** (*Prakopa*) and **pacification** (*Prashama*) of *Doṣa*. Such cyclical changes may alter susceptibility to toxic insults. [5]

**Table 2: Seasonal *Doṣa* Dominance periods**

<i>Doṣa</i>	Accumulation ( <i>Chaya</i> )	Aggravation ( <i>Prakopa</i> )	Pacification ( <i>Prashama</i> )
<i>Kapha</i>	Winter	Spring	Summer
<i>Pitta</i>	Rainy season	Autumn	Winter
<i>Vāta</i>	Summer	Rainy season	Autumn

Figure 2: Seasonal *Doṣa* Variations periods [20]



These temporal variations strongly resemble modern concepts of chronobiological adaptation.

### Concept of *Viṣa Vega*

*Viṣa Vega* refers to the sequential stages of toxic spread and manifestation within the body. [7] Classical Ayurvedic toxicology explains that poison rapidly spreads through channels (*Srotas*), disturbs *Doṣa* and produces systemic manifestations.

According to Ayurvedic descriptions, progression of poison depends upon

- Strength of poison (*Viṣa Bala*)
- Strength of patient (*Deha Bala*)
- Digestive fire (*Agni*)
- Tissue resistance
- Time of exposure (*Kāla*)
- Route of entry

The concept of *Vega* may be interpreted as dynamic toxic progression influenced by physiological rhythms.

### Correlation Between Chronotoxicology and *Viṣa Vega*

#### 1. Circadian Influence on Absorption

Modern studies show that gastrointestinal motility, pH, enzyme activity and mucosal permeability vary according to circadian timing. [14] During *Kapha Kāla*, slower digestion and higher mucus activity may delay toxic absorption, whereas *Pitta Kāla* with heightened metabolic activity may accelerate systemic spread.

#### 2. Hepatic Detoxification and *Pitta*

The liver demonstrates strong circadian oscillation in xenobiotic metabolism. [15] Cytochrome P450 (CYP) enzyme activity varies across the day. Ayurveda considers *Pitta* responsible for metabolic transformation. Increased *Pitta* periods may correspond to enhanced biochemical activity and altered toxin metabolism.

### 3. *Neurological Toxicity and Vāta*

Circadian alterations influence neurotransmission, autonomic regulation and neuronal excitability. [16] Since *Vāta* governs neural conduction and movement, toxic manifestations such as tremors, convulsions, pain and paralysis may intensify during *Vāta*-dominant periods.

### 4. *Immune Response and Kapha*

Inflammatory cytokines and immune mediators exhibit circadian variation. [17] *Kapha* is associated with stability, immunity and tissue protection. Reduced *Kapha Bala* during chronodisruption may enhance toxic vulnerability.

### 5. *Oxidative Stress and Temporal Biology*

Reactive oxygen species generation and antioxidant defense fluctuate rhythmically. [18] Melatonin secretion during night exerts antioxidant protection. Sleep deprivation and circadian disruption increase oxidative injury, potentially aggravating *Viṣa Vega*.

### Chronodisruption and Toxic Susceptibility

Modern lifestyle patterns frequently disturb biological rhythms. Shift work, excessive screen exposure, irregular meals and sleep deprivation produce circadian misalignment. [19]

Consequences include

- Impaired hepatic detoxification
- Increased oxidative stress
- Hormonal imbalance
- Reduced immunity
- Neuro-inflammation
- Metabolic dysfunction

Ayurveda similarly warns against *Prajñāparādha*, improper lifestyle and disturbance of natural rhythms. [5] Such factors may predispose individuals to severe toxic manifestations.

### Chronotherapeutic Implications in *Agada Tantra*

The integration of chronobiology with Ayurvedic toxicology may improve clinical outcomes.

#### Possible Applications

#### 1. *Timely Administration of Agada*

Administration of antidotal formulations during optimal metabolic periods may improve efficacy.

#### 2. *Circadian Detoxification Support*

Supporting liver function during peak detoxification phases may reduce toxic burden.

#### 3. *Sleep and Recovery*

Restoration of circadian rhythm may enhance tissue repair and immune recovery.

#### 4. *Personalized Toxicological Assessment*

Considering *Prakṛti*, biological rhythm and exposure timing may improve individualized management.

### Integrative Perspectives

Several parallels can be identified between Ayurveda and modern chronobiology

**Table 3: Ayurveda and modern co-relation(s)**

<i>Modern Concept</i>	<i>Ayurvedic Correlation</i>
Circadian rhythm	<i>Kāla Chakra</i>
Biological clock	<i>Doṣa Kāla</i>
Chronotoxicity	<i>Viṣa Vega</i> variation
Chronotherapy	Timed <i>Agada</i> administration
Chronodisruption	<i>Prajñāparādha</i> and <i>Asatmya</i> lifestyle

These similarities indicate that Ayurveda had an advanced understanding of temporal physiology long before modern chronobiology emerged.

### Discussion

The present review demonstrated substantial conceptual overlap between chronotoxicology and Ayurvedic temporal principles. Modern research confirms that toxicity varies according to biological timing due to circadian regulation of metabolism, immunity, oxidative stress and neuroendocrine activity. [12-18]

Ayurveda describes similar temporal fluctuations through *Tridoṣa* dominance and *Kāla* physiology. The concept of *Viṣa Vega* appears particularly relevant in understanding dynamic toxic progression under varying biological conditions. [5] [6]

The association between *Pitta* and hepatic metabolism, *Vāta* and neurological manifestations and *Kapha* with immunity and stability provides a rational framework for integrative interpretation. Furthermore, Ayurvedic emphasis on regular lifestyle, sleep, diet and seasonal adaptation aligns closely with modern circadian medicine.

Although direct experimental evidence correlating *Viṣa Vega* with circadian biomarkers remains limited, emerging chronobiological research supports the plausibility of such interactions. Future interdisciplinary studies integrating molecular chronobiology, toxicology and Ayurvedic physiology may help validate these correlations scientifically.

### Conclusion

Chronotoxicology and Ayurveda share important conceptual similarities regarding temporal regulation of physiology and disease progression. Circadian rhythms significantly influence toxic absorption, metabolism, immune response and neurological activity, thereby affecting toxic severity and progression. Ayurvedic concepts of *Tridoṣa*, *Kāla* and *Viṣa Vega* provide a holistic framework for understanding these biological oscillations.

The integration of chronobiological principles with *Agada Tantra* may open new avenues for individualized toxicological assessment, preventive strategies and chronotherapeutic interventions. Further experimental and clinical research is necessary to establish evidence-based correlations between circadian biology and Ayurvedic toxicodynamics.

#### AI Use Disclosure

Language refinement assistance was utilized during manuscript preparation. The authors critically reviewed, edited and approved the final manuscript and take full responsibility for the scientific content in accordance with journal ethical policies.

#### REFERENCES:

1. Takahashi JS. Transcriptional architecture of the mammalian circadian clock. *Nat Rev Genet.* 2017 Mar;18(3):164–179. Available from: <https://www.nature.com/articles/nrg.2016.150>  
doi:10.1038/nrg.2016.150
2. Halberg F. Chronobiology and chronotoxicology. *J Toxicol Sci.* 1981;6(1):1–11.
3. Lévi F, Okyar A, Dulong S, Innominato PF, Clairambault J. Circadian timing in cancer treatments. *Annu Rev Pharmacol Toxicol.* 2010;50:377–421.  
doi:10.1146/annurev.pharmtox.48.113006.094626
4. Zhang R, Lahens NF, Ballance HI, Hughes ME, Hogenesch JB. A circadian gene expression atlas in mammals. *Proc Natl Acad Sci USA.* 2014 Nov 11;111(45):16219–16224.  
doi:10.1073/pnas.1408886111
5. Acharya YT, editor. *Charaka Samhita of Agnivesha with Ayurveda Dipika Commentary of Chakrapanidatta.* Reprint ed. Varanasi: Chaukhambha Surbharati Prakashan; 2019.
6. Murthy KRS, translator. *Ashtanga Hridayam of Vagbhata.* Vol 1. Varanasi: Chaukhambha Krishnadas Academy; 2016.
7. Acharya YT, editor. *Sushruta Samhita with Nibandha Sangraha Commentary.* Reprint ed. Varanasi: Chaukhambha Orientalia; 2018.
8. Srikantha Murthy KR. *Ashtanga Sangraha of Vagbhata.* Varanasi: Chaukhambha Orientalia; 2015.
9. Bass J, Lazar MA. Circadian time signatures of fitness and disease. *Science.* 2016 Nov 25;354(6315):994–999. doi:10.1126/science.aah4965
10. Hastings MH, Maywood ES, Brancaccio M. Generation of circadian rhythms in the suprachiasmatic nucleus. *Nat Rev Neurosci.* 2018 Aug;19(8):453–469. doi:10.1038/s41583-018-0026-z
11. Potter GDM, Skene DJ, Arendt J, Cade JE, Grant PJ, Hardie LJ. Circadian rhythm and sleep disruption. *Occup Med.* 2016 Jan;66(1):18–23. doi:10.1093/occmed/kqv080
12. Reinberg A, Smolensky MH. Biological rhythms and medicine. *Cell Mol Life Sci.* 1983;39(4):343–353.
13. Hrushesky WJM. Circadian timing of cancer chemotherapy. *Science.* 1985;228(4695):73–75.
14. Hoogerwerf WA. Biologic clocks and the gut. *Curr Gastroenterol Rep.* 2006 Oct;8(5):353–359.
15. Panda S. Circadian physiology of metabolism. *Science.* 2016 Nov 25;354(6315):1008–1015. doi:10.1126/science.aah4967
16. Logan RW, McClung CA. Rhythms of life: Circadian disruption and brain disorders. *Nat Rev Neurosci.* 2019 Jan;20(1):49–65. doi:10.1038/s41583-018-0088-y
17. Scheiermann C, Gibbs J, Ince L, Loudon A. Clocking in to immunity. *Nat Rev Immunol.* 2018 Jul;18(7):423–437. doi:10.1038/s41577-018-0008-4
18. Reiter RJ, Tan DX, Korkmaz A, Rosales-Corral SA. Melatonin and stable circadian rhythms optimize maternal, placental and fetal physiology. *Hum Reprod Update.* 2014 Mar-Apr;20(2):293–307.



19. Karatsoreos IN. Links between circadian rhythms and psychiatric disease. *Front Behav Neurosci.* 2014 Mar 11;8:162. doi:10.3389/fnbeh.2014.00162
20. OpenAI | Research & Deployment