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REVIEW ARTICLE

Chronotherapy and its dermatological implications: A comprehensive review

Kronoterapinin gözden geçirilmesi ve dermatolojik yaklaşım: Kapsamlı bir derleme

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Abstract

Chronotherapy, the science of administering treatments in synchrony with circadian rhythms, has emerged as a promising strategy to enhance therapeutic efficacy and minimize adverse effects. Circadian rhythms govern numerous physiological processes, including immune regulation, hormone secretion, and skin barrier function. In dermatology, the skin demonstrates marked circadian variation in parameters such as transepidermal water loss (TEWL), pH, temperature, and pruritus intensity. Recent studies have shown that timing the administration of topical or systemic therapies according to these rhythms can improve outcomes in conditions such as psoriasis and atopic dermatitis. This review highlights the current understanding of circadian biology in skin physiology, the clinical relevance of chronotherapy in dermatologic diseases, and future directions for integrating chronobiology into dermatologic practice.

Keywords: Dermatology, chronotherapy, circadian rhytm.

Özet

Tedavileri sirkadiyen ritimlerle senkronize olarak uygulama bilimi olan kronoterapi, terapötik etkinliği artırmak ve olumsuz etkileri en aza indirmek için umut verici bir strateji olarak ortaya çıkmıştır. Sirkadiyen ritimler, bağışıklık düzenlemesi, hormon salgılanması ve cilt bariyeri fonksiyonu dahil olmak üzere çok sayıda fizyolojik süreci yönetir. Dermatolojide cilt, transepidermal su kaybı (TEWL), pH, sıcaklık ve pruritus yoğunluğu gibi parametrelerde belirgin sirkadiyen varyasyon gösterir. Son çalışmalar, topikal veya sistemik tedavilerin bu ritimlere göre uygulanmasının zamanlamasının sedef hastalığı ve atopik dermatit gibi durumlarda sonuçları iyileştirebileceğini göstermiştir. Bu derleme, cilt fizyolojisinde sirkadiyen biyolojinin mevcut anlayışını, dermatolojik hastalıklarda kronoterapinin klinik önemini ve kronobiyolojiyi dermatolojik uygulamaya entegre etmek için gelecekteki yönleri vurgulamaktadır.

Anahtar Kelimeler: Dermatoloji, kronoterapi, sirkadyan ritm.

INTRODUCTION

Chronotherapy is an emerging field that seeks to align the timing of medical interventions with the body's endogenous circadian rhythms in order to enhance therapeutic outcomes and reduce adverse effects. The circadian rhythm is a roughly 24-hour cycle driven by a central "clock" located in the suprachiasmatic nucleus (SCN) of the hypothalamus. This central pacemaker regulates a host of peripheral clocks present in nearly all tissues, including the liver, heart, gastrointestinal tract, and notably, the skin (1, 2).

At the molecular level, circadian rhythms are regulated by a set of core clock genes, including BMAL1, CLOCK, PER1-3, and CRY1-2, which function in autoregulatory feedback loops to maintain rhythmic expression patterns (1). These genes not only influence sleep-wake cycles but also regulate fundamental physiological processes such as metabolism, hormone secretion, immune responses, and cell proliferation (3,4). Consequently, a growing body of evidence suggests that the timing of medication administration—whether systemic or topical—can significantly alter drug absorption, metabolism, and efficacy (5).

The concept of chronotherapy is not new. It has already transformed treatment paradigms in oncology, where studies have shown that chemotherapy regimens tailored to the body's biological clock reduce toxicity and improve

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survival rates (4). Similarly, cardiovascular medicine has benefited from circadian-based approaches—for instance, administering antihypertensive medications in the evening has been shown to better control nocturnal blood pressure and lower the risk of cardiovascular events (5,6). In pulmonology, medications such as theophylline and corticosteroids for asthma have shown greater efficacy when administered according to circadian peaks in airway inflammation (7).

In recent years, attention has shifted toward the role of chronobiology in dermatology. The skin, as the body's largest organ and its first line of defense against environmental insults, exhibits pronounced circadian variation in multiple parameters: transepidermal water loss (TEWL), pH, sebum production, barrier repair, cell proliferation, and even immune surveillance (2,6). Moreover, clinical symptoms such as pruritus, erythema, and edema also show time-dependent fluctuations, often worsening at night (12).

This temporal variation in skin physiology has significant implications for the treatment of dermatologic conditions such as psoriasis, atopic dermatitis, acne, and photoaging. For instance, TEWL and skin permeability increase during the evening, potentially enhancing the penetration of topically applied drugs during these hours (10). On a molecular level, clock genes in keratinocytes and fibroblasts influence DNA repair, oxidative stress response, and the inflammatory cascade—all of which are central to the pathogenesis of chronic inflammatory skin diseases (11).

Furthermore, circadian misalignment—common in shift workers and individuals with irregular sleep patterns—has been linked to the onset and exacerbation of skin disorders. Disruption of melatonin production, for instance, impairs immune regulation and epidermal regeneration, contributing to conditions such as psoriasis and eczema (13, 14).

Given this context, the present review aims to synthesize current findings regarding the intersection of chronotherapy and dermatology. We explore how circadian rhythms impact skin biology, review the evidence supporting time-of-day-based treatment strategies for common dermatological conditions, and propose future directions for integrating chronobiological principles into routine clinical practice.

GENERAL APPROACH

General Principles of Chronotherapy

Evidence from various medical fields underscores the importance of treatment timing. In oncology, chronomodulated chemotherapy improved tolerability and efficacy in colorectal cancer patients by reducing hematologic toxicity when drugs were administered in sync with circadian rhythms (4). Similarly, morning versus evening dosing of drugs such as aspirin and theophylline results in significantly different plasma concentrations and side effect profiles (3,7).

Cardiac surgery outcomes also appear to be influenced by time of day. Montaigne et al. found that aortic valve replacement surgeries performed in the afternoon had significantly lower complication rates, possibly due to circadian fluctuations in myocardial function and inflammation (8).

Additionally, the importance of circadian rhythm in drug absorption and metabolism has been demonstrated in multiple studies (5,9), further supporting its clinical relevance beyond oncology.

Circadian Biology of the Skin

The skin demonstrates significant circadian variability in hydration, pH, TEWL, and barrier function. TEWL is higher at night, suggesting increased permeability and potential for improved drug penetration during evening hours (6). Skin temperature also follows a circadian pattern, peaking at night and dropping in the early morning (10). These physiological changes have implications for both therapeutic efficacy and symptom control.

Clock gene expression in the skin regulates cellular activities such as DNA repair, keratinocyte proliferation, and immune responses (11). These oscillations are also responsible for time-dependent variations in symptoms such as nocturnal pruritus, which is commonly observed in conditions like eczema (12).

Light perception by skin cells plays a role in circadian regulation. Melanocytes contain opsins similar to

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those in the retina, suggesting a direct sensitivity to environmental light cues (13).

CHRONOTHERAPY IN DERMATOLOGY

Psoriasis

Psoriasis is a chronic inflammatory disease influenced by circadian misalignment. Night-shift workers, who experience circadian disruption due to irregular sleep and light exposure, have a higher incidence of psoriasis, potentially due to melatonin suppression and altered immune regulation (14, 15). The vascular endothelial growth factor A (VEGF-A), which contributes to angiogenesis in psoriatic lesions, exhibits circadian variation, indicating that its expression may be time-dependent (16, 17). Chronotherapeutic inhibition of VEGF-A may enhance treatment response in psoriasis patients (18). Topical corticosteroids, the mainstay of psoriasis treatment, have shown greater efficacy when applied in the evening. Nguyen et al. demonstrated improved plaque resolution and reduced inflammation in patients using corticosteroids at night compared to those applying them in the morning (19).

Atopic Dermatitis

Atopic dermatitis (AD) symptoms often worsen at night, partly due to nocturnal increases in histamine release and barrier dysfunction (12). Cytokines like IL-4 and IL-13, key drivers in AD pathogenesis, also display circadian variation. Borghi et al. found that patients receiving dupilumab in the early afternoon experienced better symptom control and less sleep disruption than those receiving it at other times (15).

Cosmeceuticals and Topical Skin Care

Chronobiology also plays a role in cosmetic dermatology. Draelos et al. evaluated a circadian-aligned skincare system that delivers antioxidant protection in the morning and reparative peptides at night. Participants showed improved skin tone, hydration, and reduced signs of aging compared to those using conventional products (6). Chronotherapeutic strategies tailored to the circadian rhythms of the skin may enhance treatment outcomes. As illustrated in Table 1, the timing of drug administration plays a critical role in optimizing therapeutic efficacy and minimizing side effects in various dermatological conditions.

Table 1. Chronotherapy applications in dermatology

Condition	Optimal Treatment Time	Chronotherapeutic Insight
Psoriasis	Evening	Topical corticosteroids more effective in the evening due to peak inflammation
Atopic Dermatitis	Midday (12 PM - 12 AM)	Dupilumab more effective during this time window
Skin Barrier Repair	Evening/ Night	Skin permeability is higher; better absorption of moisturizers and steroids
Photoprotection	Morning/ Day	Sunscreen use aligns with UV exposure; DNA repair agents used at night
Skin Care (Cosmetic)	Evening	Improved efficacy of facial creams due to circadian rhythm of skin functions
Topical Retinoids	Evening	Increased treatment efficacy by reducing photosensitivity of topical retinoids

Chronopharmology of Topical Retinoids

Topical retinoids are widely recommended for nighttime use due to their photosensitivity, which can lead to increased skin irritation and degradation of the active compound when exposed to sunlight. Applying retinoids at night allows for maximal efficacy while minimizing potential side effects like erythema and peeling. Similarly, oral collagen supplements, which have gained popularity for their potential benefits on skin elasticity, hydration, and overall dermal structure, are also commonly taken in the evening. Although collagen absorption is not directly affected by the time of day, nighttime intake

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aligns with the body's natural repair and regeneration processes, which are most active during sleep. This circadian alignment may enhance the bioavailability and integration of collagen peptides into the skin matrix.

DISCUSSION

Chronotherapy offers a promising frontier in personalized dermatology. The circadian regulation of skin physiology provides a rational basis for optimizing treatment timing. Incorporating time-of-day considerations into therapeutic plans could enhance the efficacy of topical and systemic treatments, particularly in chronic inflammatory diseases such as psoriasis and atopic dermatitis.

Despite strong preclinical and emerging clinical data, the integration of chronotherapy into dermatology remains limited. Factors such as patient compliance, treatment complexity, and lack of standardized protocols present barriers. However, wearable circadian trackers and digital health platforms may soon allow clinicians to tailor treatments based on an individual's chronotype and real-time biological rhythms.

Furthermore, future research should explore time-of-day-dependent gene expression in skin diseases, as well as chronopharmacokinetics for dermatologic medications. Multicenter randomized trials are essential to establish best practices for treatment timing in dermatology.

Understanding and harnessing the skin's biological rhythms could revolutionize how we treat dermatologic conditions—transforming not just what we prescribe, but when we prescribe it.

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References

1. Lyons AB, Moy L, Moy R, Tung R. Circadian rhythm and the skin: a review of the literature. J Clin Aesthet Dermatol. 2019;12(9):42-5.
2. Greener M. Update on chronotherapy: it's about time. Prescriber. 2023;34:16-20.
3. Haus E, Halberg F, Cardoso SS. Increased tolerance of leukemic mice to arabinosyl cytosine with schedule adjusted to circadian system. Science. 1972;177(4043):80-2.
4. Lévi F, Okyar A, Dulong S, Innominato PF, Clairambault J. Circadian timing in cancer treatments. Annu Rev Pharmacol Toxicol. 2010;50:377-421.
5. Lemmer B. The clinical relevance of chronopharmacology in therapeutics. Pharmacol Res. 1996;33(2):107-15.
6. Draelos ZD, Makino ET, Kadoya K, Nguyen A, Jiang LI, Mehta RC. Clinical benefits of circadian-based antioxidant protection and repair. J Drugs Dermatol. 2020;19(12):1209-14.
7. Ohdo S. Chronotherapeutic strategy: rhythm monitoring, manipulation and disruption. Adv Drug Deliv Rev. 2010;62(9-10):859-75.
8. Montaigne D, Marechal X, Modine T, Coisne A, Mouton S, Fayad G. Daytime variation of perioperative myocardial injury in cardiac surgery. Lancet. 2018;391:59-69.
9. Smolensky MH. Clinical chronobiology and chronotherapeutics with applications to cardiovascular medicine. Am J Hypertens. 1997;9(4 Pt 3):11S-21S.
10. Le Fur I. Daily variations in cutaneous microcirculation: implications for skin blood flow and temperature. J Invest Dermatol. 2001;117(5):1216-20.
11. Geyfman M, Kumar V, Liu Q, Ruiz R, Gordon W, Espitia F, et al. Brain and muscle Arnt-like protein-1 (BMAL1) controls circadian cell proliferation and susceptibility to UVB-induced DNA damage in the epidermis. PNAS. 2012;109(29):11758-63.
12. Patel T, Ishiuji Y, Yosipovitch G. Nocturnal itch: why do we itch at night? Acta Derm Venereol. 2007;87(4):295-8.
13. Kleszczynski K, Fischer TW. Melatonin and human skin aging. Dermatoendocrinol. 2012;4(3):245-52.
14. Scheer FA, Hilton MF, Mantzoros CS, Shea SA. Adverse metabolic and cardiovascular consequences of circadian misalignment. PNAS.2009;106(11):4453-8.
15. Borghi A, Flacco ME, Bocchi C, Schettini N, Arlotti E, Manfredini R, et al. Time of day of biological treatment administration and outcomes in atopic dermatitis. Dermatitis. 2024.
16. Ferrara N. Vascular endothelial growth factor. Arterioscler Thromb Vasc Biol. 2009;29(6):789-91.

Turk J Clin Res. 2025;1(1):52-56
https://doi.org/10.63909/1453007

17. Marina ME, Roman II, Constantin AM, Mihu CM, Tătaru AD. Vascular endothelial growth factor involvement in psoriasis. Clujul Med. 2015;88(3):247-52.
18. Ch Chen Y, Tai Z, Zhu C, Yu Q, Zhu Q, Chen Z. VEGFA Inhibition: An effective treatment strategy for psoriasis. Int J Mol Sci. 2023;25(1):59.
19. Nguyen S, Bahakeem H, Alkhalifah A, Cavalié M, Boukari F, Montaudié H, et al. Evening corticosteroid application is more effective in psoriasis. J Eur Acad Dermatol Venereol. 2017;31(5):263-4.