

# Medicinal Cannabis and Sleep Improvement in Menopausal Women: Integrating Nocturia, Genitourinary Syndrome of Menopause, and Endocannabinoid Regulation

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## ABSTRACT

Sleep disturbances represent one of the most prevalent and disruptive symptoms experienced during menopause, affecting nearly half of women during the menopausal transition. Hormonal changes associated with declining estrogen and progesterone levels contribute to vasomotor symptoms, mood disturbances, and genitourinary syndrome of menopause (GSM), which includes urinary frequency and nocturia. These factors collectively lead to fragmented sleep and reduced sleep quality. Recently, medicinal cannabis has emerged as a potential therapeutic option for sleep disorders due to its interaction with the endocannabinoid system, which plays a key role in circadian regulation and sleep physiology. This review examines current evidence regarding sleep disturbances in menopausal women, emphasizing the combined impact of nocturia and hormonal changes. It also explores the therapeutic roles of vaginal estrogen therapy for urinary symptoms and cannabinoid-based treatments for sleep regulation. The integration of these approaches may provide a novel strategy for improving sleep quality and overall quality of life in menopausal women. Despite promising evidence, clinical trials specifically evaluating cannabis based therapies in menopausal populations remain limited. Future translational research should prioritize interdisciplinary studies that integrate neuroendocrinology, urology, and sleep medicine to develop targeted interventions for menopausal sleep disorders.

## Keywords

Menopause, Insomnia, Nocturia, Medicinal Cannabis, Cannabinoids, Genitourinary syndrome of menopause, Sleep disorders, Translational medicine.

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## Introduction

Menopause represents a major physiological transition in women's lives, typically occurring between 45 and 55 years of age. The cessation of ovarian follicular activity leads to a decline in circulating estrogen and progesterone levels, producing a range of systemic symptoms that affect physical, psychological, and neurological health. Among these symptoms, sleep disturbances are among the most frequently reported and significantly affect quality of life [1].

Insomnia during menopause is often characterized by difficulty initiating sleep, frequent awakenings, and early morning awakening. Studies suggest that approximately 40–60% of menopausal women experience clinically significant sleep problems [2]. These disturbances may arise from vasomotor symptoms such as hot flashes and night sweats, mood disorders, or changes in circadian regulation.

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Another important but often underrecognized contributor to sleep disruption during menopause is nocturia—the need to wake during the night to urinate. Nocturia is frequently associated with the genitourinary syndrome of menopause (GSM), a condition caused by estrogen deficiency affecting the vaginal epithelium, urethra, and bladder [3]. Repeated awakenings to urinate disrupt sleep cycles and prevent the restoration of deep sleep stages.

Traditional therapeutic approaches include hormone replacement therapy (HRT), sedative medications, and behavioral interventions. However, concerns about the risks associated with systemic hormone therapy and the side effects of sedative medications have prompted increasing interest in alternative therapies.

Medicinal cannabis has recently emerged as a potential therapeutic option for sleep disorders. Cannabinoids derived from *Cannabis sativa*, particularly tetrahydrocannabinol (THC) and cannabidiol (CBD), interact with the endocannabinoid system, which regulates sleep, mood, and circadian rhythms [4]. Clinical trials have suggested that cannabinoid-based therapies may improve sleep quality and reduce insomnia symptoms.

This review examines the interplay between menopause, nocturia, and sleep disturbances, and evaluates emerging evidence regarding the potential role of medicinal cannabis as part of an integrative therapeutic strategy.

### **Hormonal Regulation of Sleep During Menopause**

Sleep is regulated by complex neuroendocrine mechanisms involving circadian rhythms, neurotransmitter systems, and hormonal signaling. Estrogen and progesterone play important roles in sleep regulation by influencing thermoregulation, mood, and neurotransmitter activity.

Estrogen affects sleep by modulating serotonin and gamma-aminobutyric acid (GABA) pathways in the brain, which are involved in sleep initiation and maintenance [5]. Progesterone also has sedative properties through its interaction with GABA receptors.

During menopause, declining levels of these hormones can lead to increased sleep latency, reduced slow-wave sleep, and increased nighttime awakenings. In addition, thermoregulatory instability contributes to vasomotor symptoms such as hot flashes, which often occur at night and disrupt sleep.

These physiological changes explain why insomnia prevalence increases significantly during the menopausal transition.

### **Genitourinary Syndrome of Menopause and Nocturia**

Genitourinary syndrome of menopause encompasses a range of symptoms affecting the lower urinary tract and genital tissues, including vaginal dryness, urinary urgency, and nocturia. These symptoms arise from estrogen deficiency, which leads to thinning of the vaginal epithelium, decreased blood flow, and reduced

elasticity of urogenital tissues [3].

Nocturia is particularly disruptive because it fragments sleep architecture. Women may awaken several times during the night to urinate, preventing the completion of normal sleep cycles. Research suggests that nocturia affects nearly half of postmenopausal women and is strongly associated with insomnia and daytime fatigue [6].

Local estrogen therapy is considered one of the most effective treatments for GSM-related urinary symptoms. Vaginal estrogen creams, tablets, or rings improve urogenital tissue integrity, increase urethral closure pressure, and reduce urinary frequency. Clinical studies have demonstrated that topical estrogen therapy significantly reduces nocturia and improves urinary symptoms in postmenopausal women [7].

Improved bladder function may indirectly enhance sleep quality by reducing nighttime awakenings.

### **Impact of Nocturia on Sleep Architecture**

Sleep architecture consists of alternating stages of non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. Restorative sleep depends on the uninterrupted progression through these stages.

Nocturia disrupts this process by forcing repeated awakenings, preventing the body from reaching deeper stages of sleep. Fragmented sleep leads to reduced slow-wave sleep and increased daytime fatigue [8].

Studies have shown that individuals experiencing nocturia often report lower sleep efficiency and poorer subjective sleep quality compared with individuals without nighttime urinary symptoms [6]. In menopausal women, nocturia may interact with other symptoms such as hot flashes, further worsening sleep disturbances.

### **The Endocannabinoid System and Sleep Regulation**

The endocannabinoid system (ECS) consists of endogenous cannabinoids, cannabinoid receptors (CB1 and CB2), and enzymes responsible for their synthesis and degradation. This system plays an important role in regulating appetite, mood, pain perception, and sleep.

CB1 receptors are widely distributed throughout the central nervous system, particularly in regions involved in sleep regulation such as the hypothalamus and brainstem. Activation of these receptors can influence sleep onset and sleep duration [4].

Experimental studies suggest that cannabinoids may increase slow-wave sleep and reduce sleep latency. In addition, cannabinoids may influence circadian rhythms by modulating neurotransmitter systems involved in sleep regulation.

### **Clinical Evidence of Cannabinoids for Sleep Disorders**

Several clinical studies have evaluated the effectiveness of

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cannabinoid-based therapies for insomnia.

A randomized double-blind crossover trial demonstrated that a medicinal cannabis oil containing THC and CBD significantly improved sleep quality and reduced insomnia severity among adults with chronic insomnia [9].

Other clinical studies have shown that cannabidiol may reduce anxiety and improve sleep in patients experiencing insomnia or stress-related sleep disturbances [10].

Systematic reviews have also found modest improvements in sleep outcomes among individuals using cannabinoid-based therapies [11]. However, these studies were not specifically conducted in menopausal populations.

### Cannabis Use Among Menopausal Women

Recent surveys suggest that cannabis use among menopausal women is increasing, particularly for the management of sleep disturbances, anxiety, and pain [12].

Many women report using cannabis products such as oils, edibles, or tinctures to improve sleep quality. Some observational studies suggest that cannabis may also reduce the severity of vasomotor symptoms.

Despite growing interest, controlled clinical trials evaluating cannabis use specifically among menopausal women remain limited.

### Discussion

#### Integrative Therapeutic Strategies

Sleep disturbances during menopause often result from the interaction of multiple physiological systems, including endocrine, neurological, and urogenital pathways. As a result, treatments targeting a single mechanism may not fully resolve symptoms.

Vaginal estrogen therapy effectively addresses urinary symptoms such as nocturia by restoring urogenital tissue function. At the same time, cannabinoid-based therapies may regulate central nervous system pathways involved in sleep and stress regulation.

Combining these approaches could provide a more comprehensive therapeutic strategy for menopausal women experiencing insomnia. However, rigorous clinical trials are needed to evaluate the safety and efficacy of such integrated treatments.

#### Future Research Directions

Future research should focus on:

1. Randomized clinical trials evaluating cannabinoids in menopausal women
2. Standardization of cannabinoid formulations and dosages
3. Long-term safety evaluations in middle-aged and older women
4. Studies investigating interactions between cannabinoid therapy and hormone therapy

5. Biomarker studies examining endocannabinoid signaling during menopause

Such research would contribute to the development of targeted therapies for menopausal sleep disorders.

### Conclusion

Sleep disturbances are among the most common and disruptive symptoms experienced during menopause. Hormonal changes, nocturia, and vasomotor symptoms collectively contribute to fragmented sleep and reduced quality of life. Vaginal estrogen therapy effectively reduces urinary symptoms associated with GSM, including nocturia, while emerging evidence suggests that cannabinoid-based therapies may improve sleep regulation. Although medicinal cannabis represents a promising therapeutic option, further clinical research is needed to establish its role in menopause management.

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