



ROLE OF PROCYANIDIN B-2 AS ANTIOXIDANT AND ANTI-INFLAMMATORY AGENT IN CONTROLLING INSOMNIA

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ABSTRACT

Background: Insomnia, a prevalent sleep disorder characterized by difficulties in initiating or maintaining sleep, affects millions globally and can lead to significant health issues, including cognitive impairments, mood disorders, and weakened immunity. Traditional treatments, while effective, often have adverse side effects, prompting the need for alternative remedies. Procyanidin B-2, a naturally occurring antioxidant found in *Prunus cerasus* (sour cherry) fruit, has emerged as a potential natural solution for insomnia.

Result and Discussion: This review explores the mechanisms by which Procyanidin B-2 may control insomnia, by its antioxidant and anti-inflammatory properties. The Said properties may lead to modulation of neurotransmitters, and regulation of circadian rhythms. Preclinical studies demonstrate that Procyanidin B-2 can improve sleep latency, duration, and quality. Limited clinical trials and anecdotal evidence further suggest its efficacy, particularly in enhancing sleep duration and reducing disturbances. Despite its promise, comprehensive clinical trials are necessary to confirm these findings and establish standardized dosages. Procyanidin B-2's safety profile is generally positive, with minimal side effects. Practical applications include dietary incorporation of Procyanidin B-2-rich foods such as sour cherries, apples, and cocoa, as well as supplements and functional foods. Future research should focus on detailed mechanistic studies and the development of advanced formulations to enhance bioavailability.

Conclusion: Procyanidin B-2 represents a promising natural alternative for managing insomnia, potentially offering a safe, effective, and holistic approach to improving sleep health.

KEYWORDS:	Antioxidant, Insomnia, Procyanidin B-2, Prunus cerasus, sleep disorder
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INTRODUCTION

Insomnia, a common sleep disorder characterized by difficulty in falling asleep, staying asleep, or waking up too early, affects millions of people worldwide. The condition can lead to severe health consequences, including cognitive impairment, mood disorders, and a weakened immune system. Traditional treatments for insomnia include pharmacological interventions and behavioral therapies. However, these treatments often come with side effects or limitations, prompting the exploration of alternative remedies. One such potential remedy is Procyanidin B-2, a naturally occurring antioxidant found in *Prunus cerasus* (sour cherry) fruit. This article delves into the potential role of Procyanidin B-2 in managing insomnia, examining its mechanisms of action, current research, and implications for future therapeutic use.¹²³

Understanding Insomnia

Causes and Consequences

Insomnia can be caused by a variety of factors, including stress, anxiety, depression, chronic pain, and lifestyle habits. Additionally, environmental factors such as noise, light, and temperature can contribute to the disorder. The consequences of insomnia are far-reaching, impacting both physical and mental health. Chronic insomnia has been linked to an increased risk of cardiovascular disease, diabetes, obesity, and mental health disorders such as depression and anxiety.⁴

Current Treatments

The primary treatments for insomnia include cognitive-behavioral therapy for insomnia (CBT-I) and pharmacological interventions such as benzodiazepines, non-benzodiazepine hypnotics, and melatonin receptor agonists. While these treatments can be effective, they often come with side effects such as dependency, tolerance, and residual daytime drowsiness. Additionally, they may not address the underlying causes of insomnia, highlighting the need for alternative treatments.⁵

¹ Cásedas G, Les F, López V. Anthocyanins: Plant pigments, food ingredients or therapeutic agents for the CNS? A mini-review focused on clinical trials. *Current Pharmaceutical Design*. 2020 May 1;26(16):1790-8.

² Santos HO, Genario R, Gomes GK, Schoenfeld BJ. Cherry intake as a dietary strategy in sport and diseases: a review of clinical applicability and mechanisms of action. *Critical Reviews in Food Science and Nutrition*. 2021 Feb 4;61(3):417-30.

³ Sharma P, Kumar A, Singh D. Dietary flavonoids interaction with CREB-BDNF pathway: An unconventional approach for comprehensive management of epilepsy. *Current neuropharmacology*. 2019 Dec 1;17(12):1158-75.

⁴ Bonnet MH, Arand DL. Hyperarousal and insomnia: state of the science. *Sleep medicine reviews*. 2010 Feb 1;14(1):9-15.

⁵ Spielman AJ, Caruso LS, Glovinsky PB. A behavioral perspective on insomnia treatment. *Psychiatric Clinics of North America*. 1987 Dec 1;10(4):541-53.

Procyanidin B-2: An Overview

Chemical Structure and Properties

Procyanidin B-2 is a type of flavonoid, specifically a proanthocyanidin, found in various plants, including *Prunus cerasus*. Its chemical structure consists of two epicatechin molecules linked by a 4→8 bond. This compound is known for its potent antioxidant properties, which help in neutralizing free radicals and reducing oxidative stress.⁶

Sources of Procyanidin B-2

Procyanidin B-2 is abundant in several plant sources, including apples, grapes, cocoa, and particularly in *Prunus cerasus* (sour cherry) fruit. The concentration of Procyanidin B-2 in these fruits can vary depending on the cultivation conditions, ripeness, and processing methods.⁷

Mechanisms of Action

Antioxidant Activity

One of the primary mechanisms by which Procyanidin B-2 exerts its effects is through its antioxidant activity. Oxidative stress, caused by an imbalance between free radicals and antioxidants in the body, is implicated in various diseases, including sleep disorders like insomnia. By scavenging free radicals, Procyanidin B-2 helps in reducing oxidative stress, which may contribute to improved sleep quality.⁸

Anti-inflammatory Effects

Chronic inflammation is another factor that can contribute to sleep disturbances. Procyanidin B-2 has been shown to possess anti-inflammatory properties, potentially modulating the production of pro-inflammatory cytokines and reducing inflammation. This anti-inflammatory action can help alleviate symptoms associated with insomnia, particularly in individuals with underlying inflammatory conditions.⁹

Modulation of Neurotransmitters

Sleep regulation is intricately linked to the balance of neurotransmitters in the brain. Procyanidin B-2 may influence the levels of key neurotransmitters such as serotonin, dopamine, and gamma-

⁶ Appeldoorn MM. Dietary A-and B-type procyanidins: characterization and biofunctional potential of an abundant and diverse group of phenolics. Wageningen University and Research; 2009.

⁷ Zineb OY, Rashwan AK, Karim N, Lu Y, Tangpong J, Chen W. Recent developments in procyanidins on metabolic diseases, their possible sources, pharmacokinetic profile, and clinical outcomes. *Food Reviews International*. 2023 Sep 8;39(8):5255-78.

⁸ Spranger I, Sun B, Mateus AM, de Freitas V, Ricardo-da-Silva JM. Chemical characterization and antioxidant activities of oligomeric and polymeric procyanidin fractions from grape seeds. *Food chemistry*. 2008 May 15;108(2):519-32.

⁹ Martinez-Micaelo N, González-Abuín N, Pinent M, Ardévol A, Blay M. Procyanidin B2 inhibits inflammasome-mediated IL-1 β production in lipopolysaccharide-stimulated macrophages. *Molecular nutrition & food research*. 2015 Feb;59(2):262-9.

aminobutyric acid (GABA), which play crucial roles in sleep-wake cycles. By modulating these neurotransmitters, Procyanidin B-2 could potentially promote better sleep quality and reduce symptoms of insomnia.¹⁰

Regulation of Circadian Rhythms

Circadian rhythms, the body's internal clock regulating the sleep-wake cycle, can be disrupted by various factors, leading to insomnia. Procyanidin B-2 may help in regulating circadian rhythms by influencing the expression of clock genes and improving the synchronization of the sleep-wake cycle. This regulatory effect can enhance sleep quality and duration.¹¹

Research on Procyanidin B-2 and Insomnia

Preclinical Studies

Several preclinical studies have investigated the effects of Procyanidin B-2 on sleep patterns and insomnia. Animal models have shown that administration of Procyanidin B-2 can improve sleep latency, increase sleep duration, and enhance overall sleep quality. These studies suggest that the compound may have potential as a natural sleep aid.¹²

Clinical Trials

While preclinical studies are promising, clinical trials on the effects of Procyanidin B-2 on insomnia are limited. However, some studies have explored the impact of sour cherry juice, which contains high levels of Procyanidin B-2, on sleep quality. These trials have reported improvements in sleep duration and efficiency, indicating the potential benefits of Procyanidin B-2 for individuals with insomnia.¹³

Case Studies and Anecdotal Evidence

In addition to clinical trials, anecdotal evidence and case studies have highlighted the potential benefits of Procyanidin B-2 for sleep. Individuals who have consumed sour cherry products have reported improvements in sleep quality, reduced sleep latency, and fewer awakenings during the

¹⁰ Koizumi R, Fushimi T, Sato Y, Fujii Y, Sato H, Osakabe N. Relationship between hemodynamic alteration and sympathetic nerve activation following a single oral dose of cinnamtannin A2. *Free radical research*. 2021 May 4;55(5):491-8.

¹¹ Losso JN, Finley JW, Karki N, Liu AG, Prudente A, Tipton R, Yu Y, Greenway FL. Pilot study of the tart cherry juice for the treatment of insomnia and investigation of mechanisms. *American journal of therapeutics*. 2018 Mar 1;25(2):e194-201.

¹² Losso JN, Finley JW, Karki N, Liu AG, Prudente A, Tipton R, Yu Y, Greenway FL. Pilot study of the tart cherry juice for the treatment of insomnia and investigation of mechanisms. *American journal of therapeutics*. 2018 Mar 1;25(2):e194-201.

¹³ Cásedas G, Les F, López V. Anthocyanins: Plant pigments, food ingredients or therapeutic agents for the CNS? A mini-review focused on clinical trials. *Current Pharmaceutical Design*. 2020 May 1;26(16):1790-8.

night. While these reports are encouraging, further research is needed to establish the efficacy of Procyanidin B-2 in managing insomnia.¹⁴

Potential Benefits of Procyanidin B-2 for Insomnia

Improved Sleep Quality

One of the primary benefits of Procyanidin B-2 is its potential to improve sleep quality. By reducing oxidative stress and inflammation, and modulating neurotransmitter levels, Procyanidin B-2 can promote a more restful and uninterrupted sleep. This improvement in sleep quality can have a significant impact on overall health and well-being.¹⁵

Reduced Sleep Latency

Procyanidin B-2 may also help in reducing sleep latency, the time it takes to fall asleep. By promoting relaxation and reducing anxiety, the compound can facilitate the onset of sleep, helping individuals with insomnia to fall asleep more quickly.¹⁶

Enhanced Sleep Duration

In addition to improving sleep quality and reducing sleep latency, Procyanidin B-2 may enhance sleep duration. Longer sleep duration can help individuals achieve the recommended amount of sleep, leading to better physical and mental health.¹⁷

Fewer Sleep Disturbances

By regulating circadian rhythms and modulating neurotransmitter levels, Procyanidin B-2 can help in reducing sleep disturbances such as awakenings during the night. Fewer sleep disturbances can lead to more restorative sleep and improved daytime functioning.¹⁸

Safety and Side Effects

Toxicity Studies

Toxicity studies on Procyanidin B-2 have indicated that the compound is generally safe for consumption. Animal studies have shown no significant adverse effects at doses commonly

¹⁴ Wang W, Liu T, Ding Y, Zhang Y. Effects of polyphenol-rich interventions on sleep disorders: A systematic review and meta-analysis. *Current Research in Food Science*. 2023 Jan 1;6:100462.

¹⁵ Cásedas G, Les F, López V. Anthocyanins: Plant pigments, food ingredients or therapeutic agents for the CNS? A mini-review focused on clinical trials. *Current Pharmaceutical Design*. 2020 May 1;26(16):1790-8.

¹⁶ Wang W, Liu T, Ding Y, Zhang Y. Effects of polyphenol-rich interventions on sleep disorders: A systematic review and meta-analysis. *Current Research in Food Science*. 2023 Jan 1;6:100462.

¹⁷ Di Lorenzo C, Colombo F, Biella S, Stockley C, Restani P. Polyphenols and human health: The role of bioavailability. *Nutrients*. 2021 Jan 19;13(1):273.

¹⁸ Kolodziej H. 7 th Tannin Conference (Presymposium) and 58 th International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research. *Planta Med*. 2010;76:1163-374.

found in dietary sources. However, long-term studies in humans are needed to establish the safety profile of Procyanidin B-2.¹⁹

Potential Side Effects

While Procyanidin B-2 is considered safe, some individuals may experience mild side effects such as gastrointestinal discomfort or allergic reactions. It is important to consume the compound in moderation and consult with a healthcare provider before using it as a sleep aid.²⁰

Practical Applications

Dietary Sources

Incorporating dietary sources of Procyanidin B-2, such as sour cherries, apples, grapes, and cocoa, into the diet can provide a natural way to enhance sleep quality. Consuming these foods regularly can help in obtaining the benefits of Procyanidin B-2 without the need for supplements.²¹

Supplements

Procyanidin B-2 supplements are available in various forms, including capsules, tablets, and powders. These supplements can provide a concentrated dose of the compound, offering a convenient option for individuals seeking to improve their sleep. However, it is important to choose high-quality supplements from reputable sources.²²

Functional Foods and Beverages

The development of functional foods and beverages enriched with Procyanidin B-2 offers another practical application. Products such as sour cherry juice, teas, and fortified snacks can provide an easy and enjoyable way to incorporate Procyanidin B-2 into the diet.²³

Future Research Directions

Mechanistic Studies

¹⁹ Takahashi T, Yokoo Y, Inoue T, Ishii A. Toxicological Studies on Procyanidin B-2 for External Application as a Hair Growing Agent. *Food and Chemical Toxicology*. 1999 May 1;37(5):545-52.

²⁰ Wu J, Huang W, Xiao H, Xie Y, Yuan Z, Yi J, Chen J, Tu D, Tian Y. Procyanidins B2 reverses the T-2 toxin-induced mitochondrial apoptosis in TM3 Leydig cells. *Journal of Functional Foods*. 2018 Jun 1;45:118-28.

²¹ Xiao Y, Yang C, Xu H, Wu Q, Zhou Y, Zhou X, Miao J. Procyanidin B2 prevents dyslipidemia via modulation of gut microbiome and related metabolites in high-fat diet fed mice. *Journal of Functional Foods*. 2020 Dec 1;75:104285.

²² Xiao Y, Dong J, Yin Z, Wu Q, Zhou Y, Zhou X. Procyanidin B2 protects against d-galactose-induced mimetic aging in mice: Metabolites and microbiome analysis. *Food and Chemical Toxicology*. 2018 Sep 1;119:141-9.

²³ Gonthier MP, Donovan JL, Texier O, Felgines C, Remesy C, Scalbert A. Metabolism of dietary procyanidins in rats. *Free Radical Biology and Medicine*. 2003 Oct 15;35(8):837-44.

Further research is needed to elucidate the precise mechanisms by which Procyanidin B-2 influences sleep. Mechanistic studies can help in understanding the molecular pathways involved and identify potential targets for therapeutic intervention.

Clinical Trials

More robust clinical trials are required to establish the efficacy of Procyanidin B-2 in managing insomnia. These trials should include larger sample sizes, longer durations, and standardized dosages to provide more conclusive evidence.

Formulation Development

The development of novel formulations and delivery systems for Procyanidin B-2 can enhance its bioavailability and efficacy. Innovative approaches such as nanotechnology and encapsulation can improve the stability and absorption of the compound, making it more effective as a sleep aid.

Conclusion

Procyanidin B-2, a potent antioxidant found in *Prunus cerasus* (sour cherry) fruit, holds significant potential as a natural remedy for insomnia. Its antioxidant, anti-inflammatory, and neurotransmitter-modulating properties make it a promising candidate for improving sleep quality, reducing sleep latency, and enhancing sleep duration. While preclinical studies and anecdotal evidence are encouraging, further clinical trials and mechanistic studies are needed to fully understand the benefits and safety of Procyanidin B-2 for insomnia. Incorporating dietary sources of Procyanidin B-2 and exploring functional foods and supplements can provide practical ways to harness its sleep-promoting effects. As research continues to evolve, Procyanidin B-2 may emerge as a valuable addition to the arsenal of natural sleep aids, offering a safe and effective solution for individuals struggling with insomnia.

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