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Novel Formula Containing Melatonin Precursors for Sleep Regulation

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HIGHLIGHTS

- Melatonin precursor formula improves sleep quality in patients with sleep disorders.
- New formulation reduces time to fall asleep and nighttime awakenings.
- Significant improvement in overall sleep satisfaction after 30 days of use.
- Disparities in sleep aspects narrowed with the use of the melatonin precursor formula.

Abstract: This study aimed to assess the efficacy of a new formulation containing melatonin precursors in patients with sleep disorders. Thirty-six individuals were divided into two groups: one receiving the new formulation and the other a placebo, for 30 days. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI) questionnaire before and after intervention. It showed significant improvements in sleep quality, including reduced time to fall asleep, fewer nighttime awakenings, and higher overall satisfaction, in the group receiving the new formulation. However, some aspects, such as difficulty staying awake during the day, did not show significant differences. Comparison between groups revealed initial disparities in sleep-related aspects, which narrowed after intervention in the formulation supplement group. These findings suggest that the new formulation may effectively improve sleep quality, emphasizing the need for further research to comprehensively understand its impact on sleep and overall health.

Keywords: Sleep disorders; Melatonin; 5-Hydroxytryptophan; Tryptophan.

INTRODUCTION

Melatonin is a hormone produced by the pineal gland in response to decreased environmental light. Its production is regulated by the circadian rhythm, a cycle of approximately 24 hours governing biological and behavioral processes in living organisms [1-3].

The pineal gland, also known as the epiphysis, is a small endocrine gland located in the center of the brain, between the cerebral hemispheres. It plays a crucial role in regulating the sleep-wake cycle and melatonin production. Specialized cells called pinealocytes synthesize and release melatonin. Melatonin production is controlled by the suprachiasmatic nucleus (SCN) of the hypothalamus, which receives information about ambient light through the eyes [3,4].

During the day, when light is present, the pineal gland is less active, and melatonin production is inhibited. As light decreases, especially at night, the SCN stimulates the pineal gland to increase melatonin production, which is released into the bloodstream [5].

Melatonin plays an important role in sleep regulation, helping to induce sleep and maintain a regular sleep-wake rhythm. Additionally, it also possesses antioxidant properties and regulates other physiological processes such as mood regulation, immune response, and hormonal regulation [1-5].

The pineal gland and melatonin production are influenced by environmental factors such as exposure to artificial light at night and exposure to sunlight during the day. Changes in sleep patterns, such as working at night or crossing different time zones, can affect melatonin production and cause sleep disorders and related health problems [3].

Melatonin is a hormone naturally produced by the body that plays a fundamental role in regulating the sleep-wake cycle. Melatonin synthesis occurs in several steps and involves different biochemical precursors. The biochemical precursors of melatonin are: a) Tryptophan: Tryptophan is an essential amino acid found in foods such as meat, fish, dairy products, eggs, nuts, and seeds. It is converted into 5-hydroxytryptophan (5-HTP) by an enzyme called tryptophan hydroxylase; b) 5-Hydroxytryptophan (5-HTP): 5-HTP is an intermediate compound in serotonin synthesis, an important neurotransmitter in the brain. The enzyme 5-hydroxytryptophan decarboxylase converts 5-HTP into serotonin; c) Serotonin: Serotonin is a neurotransmitter that plays a vital role in mood, sleep, and appetite regulation. Serotonin is then converted into N-acetylserotonin by the enzyme N-acetyltransferase; d) N-acetylserotonin (NAS): N-acetylserotonin is a key intermediate in the melatonin synthesis pathway. It is converted into melatonin by the enzyme hydroxyindole-O-methyltransferase (HIOMT); e) Melatonin is the final hormone produced in the pineal gland, located in the brain. It is synthesized from NAS by the enzyme HIOMT. Melatonin production is regulated by the circadian rhythm, being released at night in response to decreased ambient light [6-9].

Pineal gland calcification refers to the accumulation of calcium deposits in this gland, which can lead to a reduction in its function. Although calcification is a natural occurrence associated with aging, certain factors can accelerate this process, such as exposure to toxins, nutritional deficiencies, and specific medical conditions. Pineal gland calcification can affect melatonin production, impairing sleep regulation and other related processes [10].

In addition to the pineal gland, melatonin is also produced in other parts of the body, such as the gastrointestinal tract, retina, bone marrow, and blood platelets. These extrapineal sources of melatonin production may contribute to the overall levels of melatonin in the body, although the pineal gland is primarily responsible for its synthesis.

In addition to endogenous melatonin production, there are also natural sources of melatonin that can be consumed through diet. Some foods contain melatonin in varying amounts, including fruits, vegetables, grains, seeds, and seafood. However, the amount of melatonin present in these foods is generally low and varies depending on factors such as species, variety, cultivation method, and food storage. Additionally, dietary melatonin is readily degraded in the gastrointestinal tract, making the efficient absorption of this hormone through diet uncertain.

Supplementation with synthetic melatonin is a common option to increase melatonin levels in the body, especially for those who have difficulty sleeping or suffer from sleep disorders. However, it is important to consult a healthcare professional before starting any supplementation [1,4,9].

Sleep disorders are common in adults and the elderly and can have various causes. Some of the most common sleep disorders include insomnia, sleep apnea, restless leg syndrome, circadian rhythm disorders, age-related sleep disorders, and sleep disorders related to medical conditions [11-13].

The treatment of sleep disorders in adults and the elderly may vary depending on the underlying cause. Lifestyle changes, such as adopting a regular sleep routine, creating a sleep-conducive environment, and

practicing proper sleep hygiene, can help improve sleep quality. In some cases, the use of prescribed formulation supplements or specific therapies may be necessary [14].

The proposed formulation offers a novel approach compared to traditional supplements by focusing on the delivery of melatonin precursors, such as tryptophan and 5-hydroxytryptophan, rather than melatonin itself. This strategy aims to enhance the body's endogenous melatonin production, potentially leading to more physiologically aligned circadian rhythm regulation. Unlike direct melatonin supplementation, which can cause abrupt increases in hormone levels and potential desensitization, the precursor-based approach supports a gradual synthesis pathway, mimicking natural processes and reducing the likelihood of adverse effects associated with exogenous melatonin use. Additionally, the inclusion of carefully selected biochemical cofactors enhances precursor bioavailability and efficacy, positioning this formulation as a significant advancement in the field of sleep-regulating therapeutics.

Here the objectives was to supplement patients with sleep disorders with a novel formulation containing melatonin precursors and evaluate the efficiency of the proposed new formulation through clinical history and questionnaire assessment.

MATERIAL AND METHODS

Methods

Formulation for one capsule: Vitamin B5 (Pantothenic acid) 50mg, Tryptophan – 250mg, L-cysteine - 200mg.

Groups were composted by patients with sleep disorders in the clinic's routine were selected and divided into 2 major groups, one using a common placebo and the other the proposed Formulation. A daily dose for 30 days for each individual. The assessment of sleep quality was conducted using validated scientific questionnaires, which provide an objective and standardized measure of different aspects of sleep. The Pittsburgh Sleep Quality Index (PSQI) was used:

1. During the past month, at what time did you usually go to bed at night?

a) Before 8 p.m.
b) Between 8 p.m. and 9 p.m.
c) Between 9 p.m. and 10 p.m.
d) Between 10 p.m. and 11 p.m.
e) After 11 p.m.

2. During the past month, at what time did you usually wake up in the morning?

a) Before 5 a.m.
b) Between 5 a.m. and 6 a.m.
c) Between 6 a.m. and 7 a.m.
d) Between 7 a.m. and 8 a.m.
e) After 8 a.m.

3. During the past month, how long, on average, did it take you to fall asleep at night?

a) Less than 15 minutes
b) Between 16 and 30 minutes
c) Between 31 and 45 minutes
d) Between 46 and 60 minutes
e) More than 60 minutes

4. During the past month, how many times did you wake up during the night?

a) Not at all
b) Once
c) Twice
d) Three times
e) More than three times

5. During the past month, overall, how would you rate the quality of your sleep?

a) Very good
b) Good
c) Neither good nor bad
d) Bad
e) Very bad

6. During the past month, how many hours of sleep did you have on average in one night?

a) Less than 5 hours
b) Between 5 and 6 hours
c) Between 6 and 7 hours
d) Between 7 and 8 hours
e) More than 8 hours

7. During the past month, how many times did you have difficulty breathing while asleep?

a) Not at all
b) Once
c) Twice
d) Three times
e) More than three times

8. During the past month, how many times did you have trouble staying awake during daily activities?

a) Not at all
b) Once
c) Twice
d) Three times
e) More than three times

9. During the past month, how many times did you feel pain or discomfort that interfered with your sleep?

a) Not at all
b) Once
c) Twice
d) Three times
e) More than three times

10. During the past month, how would you rate your overall satisfaction with your sleep?

a) Very satisfied
b) Satisfied
c) Neither satisfied nor dissatisfied
d) Dissatisfied
e) Very dissatisfied

After answering these questions, it is possible to calculate a final score, which will indicate sleep quality. The higher the score, the worse the sleep quality. Clinical characteristics will also be evaluated.

A Clinical assessment were made. The careful and systematic approach to diagnosing and treating sleep-related problems was conducted by the postdoctoral fellow, an otolaryngologist physician. This evaluation began with anamnesis, with a detailed interview with the patient to obtain information about sleep disorder symptoms, medical history, sleep history, sleep patterns, and any triggering or aggravating factors. The second stage involved keeping a sleep diary, which basically involved daily recording of sleep quality, bedtime and wake-up times, events during the night, and any sleep-related symptoms.

Methodological questionnaire statistical procedures

This study was reviewed and approved by the Research Ethics Committee of the State University of Ponta Grossa (UEPG), ensuring compliance with ethical guidelines for research involving human participants. The project was registered under the protocol number 70958423.2.0000.0105, with the Approval Number 6.155.925, in accordance with national and international standards for ethical research, including the principles outlined in the Declaration of Helsinki.

The questionnaire was applied to 36 individuals. Of these, 19 formed the group called “without formulation supplement” and 17 correspond to the “with formulation supplement” group.

The inclusion criteria for this study required participants to be healthy adults aged 18 to 60 years, with no history of chronic illnesses, sleep disorders, or psychiatric conditions. Participants needed to have a consistent sleep routine, with no significant disruptions such as shift work or recent long-haul travel. Exclusion criteria included the use of sleep medications or supplements within the last three months, pregnancy or breastfeeding, a history of allergic reactions to any of the components in the formulation, and any medical conditions that could interfere with sleep or circadian rhythm. All participants provided informed consent prior to enrollment, ensuring voluntary participation and understanding of the study procedures.

Questions 3, 4, 5, 6, 7, 8, 9, 10 had a Likert response scale converted to a score of 1 to 5. In all cases, a score of 5 was considered for the most positive response and 1 for the least positive alternative. For example, question 3 investigates how long, on average, it takes the respondent to fall asleep at night. A score of 5 was given for alternative a) less than 15 minutes, and 1 for alternative e) more than 60 minutes. On the other hand, question 6 investigates how many hours of sleep you had on average in a night. In this case, 5 was scored for alternative e) more than 8 hours and 1 for alternative a) less than 5 hours.

For data analysis, the Shapiro-Wilk test was performed to verify the normality of the data. Considering non-normal data ($p<0.05$), the Wilcoxon test was used to compare the mean scores in each question before and after administration of the formulation supplement, in the “Without formulation supplement” and “With formulation supplement” groups. The comparison between the “Without formulation supplement” and “With formulation supplement” groups in the periods before and after the intervention was performed using the Mann Whitney test. The statistical package SPSS version 22.0 was used for the analyses, adopting a significance level of 5%.

RESULTS

The study included a total of 36 participants, composed of 16 men (44.44%) and 20 women (55.56%). Participants were divided into two groups: the “without formulation supplement” group, comprising 19 individuals (8 men, 42.10%; and 11 women, 57.90%), and the “on formulation supplement” group, consisting of 17 participants (8 men, 47.05%; and 9 women, 52.95%).

Regarding sleep behavior, prior to supplementation, most individuals reported going to bed after 11 PM (Q1). Following supplementation, a significant proportion of participants in the “on formulation supplement” group shifted their bedtime to between 10 and 11 PM, suggesting earlier sleep initiation. In terms of waking times (Q2), minor fluctuations were observed, with more participants reporting waking between 7 and 8 AM or later, indicating a slight delay in waking times post-supplementation.

The “on formulation supplement” group exhibited marked improvements across several parameters. Post-supplementation, the time taken to fall asleep (Q3), self-reported sleep quality (Q5), hours of sleep (Q6), and overall satisfaction with sleep (Q10) significantly increased, with p-values below 0.05. Conversely, occurrences of nighttime waking (Q4), difficulty staying awake during the day (Q8), and pain or discomfort interfering with sleep (Q9) decreased significantly in this group, reinforcing the formulation’s positive effect on sleep quality.

The “without formulation supplement” group displayed minimal changes in the assessed parameters, with the exception of a significant improvement in overall sleep satisfaction (Q10, $p<0.05$). These findings suggest that while both groups experienced some sleep-related benefits, the “on formulation supplement” group demonstrated more consistent and statistically significant improvements across multiple aspects of sleep quality. Tables 1 and 2 demonstrates the normality comparison before and after supplementation with the proposed formulations.

Table 1. Normality comparison before and after supplementation with the proposed formulation.

	P-VALUE	CONCLUSION
Q3	0,034	NOT NORMAL
Q4	0,041	NOT NORMAL
Q5	0,016	NOT NORMAL
Q6	0,002	NOT NORMAL
Q8	0,001	NOT NORMAL
Q9	0,001	NOT NORMAL
Q10	0,127	NORMAL
Q3 DEPOIS	0,054	NORMAL
Q4 DEPOIS	0,010	NOT NORMAL
Q5 DEPOIS	0,008	NOT NORMAL
Q6 DEPOIS	0,065	NORMAL
Q8 DEPOIS	0,001	NOT NORMAL
Q9 DEPOIS	0,001	NOT NORMAL
Q10 DEPOIS	0,016	NOT NORMAL

Table 2. Normality comparison before and after supplementation with the proposed formulation.

	P-VALUE	CONCLUSION
Q3	0,097	NORMAL
Q4	0,060	NORMAL
Q5	0,005	NOT NORMAL
Q6	0,011	NOT NORMAL
Q7	0,001	NOT NORMAL
Q8	0,038	NOT NORMAL
Q9	0,001	NOT NORMAL
Q10	0,027	NOT NORMAL
Q3 DEPOIS	0,006	NOT NORMAL
Q4 DEPOIS	0,008	NOT NORMAL
Q5 DEPOIS	0,007	NOT NORMAL
Q6 DEPOIS	0,145	NORMAL
Q7 DEPOIS	0,001	NOT NORMAL
Q8 DEPOIS	0,001	NOT NORMAL
Q9 DEPOIS	0,001	NOT NORMAL
Q10 DEPOIS	0,015	NOT NORMAL

Thirty-six individuals participated in the research, 16 (44.44%) men and 20 (55.56%) women. The “without formulation supplement” group consisted of 19 participants, 8 (42.10%) men and 11 (57.90%) women. In turn, the “on formulation supplement” group was made up of 17 interviewees, of which 8 (47.05%) were male and 9 (52.95%) were female. Table 3 presents the frequency (Questions 1 and 2) and average score before and after the responses of the “without formulation supplement” group.

Table 3. Comparison of before and after responses from the "without formulation supplement" group

		BEFORE	AFTER
Q1	BEFORE 20 h	0	0
	IN BETWEEN 20 - 21 h	0	0
	IN BETWEEN 21 - 22 h	3	3
	IN BETWEEN 22 - 23 h	6	6
	AFTER 23 ho	10	10
Q2	BEFORE 5 h	0	0
	IN BETWEEN 5 - 6 h	2	1
	IN BETWEEN 6 - 7 h	9	9
	IN BETWEEN 7 - 8 h	6	8
	AFTER 8 h	2	1
Q3		3,47 (0,96)	3,36 (1,06)
Q4		2,05 (1,35)	1,94 (1,47)
Q5		3,42 (0,83)	3,73 (0,87)
Q6		3,05 (0,70)	3,36 (1,01)
Q7		0,00 (0,00)	0,00 (0,00)
Q8		1,36 (1,73)	1,15 (1,34)
Q9		0,94 (1,39)	0,68 (1,37)
Q10		3,00 (1,00)	3,68 (1,00)

The time at which individuals reported usually going to bed (Q1) did not change before and after administration of the formulation supplement. Regarding the time at which individuals reported waking up in the morning (Q2), there were small fluctuations. In the period afterwards, the number of people who reported waking up between 7 and 8 am increased (2 people), and there was a drop among those who reported waking up between 5 and 6 am and after 8 am (1 person).

Table 4 presents the before and after comparison of the responses of the "without formulation supplement" group using the Wilcoxon test.

Table 4. Wilcoxon test before and after responses from the "no formulation supplement" group.

	BEFORE (Mean and standard deviation)	AFTER (Mean and standard deviation)	P-VALUE	CONCLUSION
Q3	3,47 (0,96)	3,36 (1,06)	0,714	H0 is accepted
Q4	2,05 (1,35)	1,94 (1,47)	0,642	H0 is accepted
Q5	3,42 (0,83)	3,73 (0,87)	0,163	H0 is accepted
Q6	3,05 (0,70)	3,36 (1,01)	0,141	H0 is accepted
Q7	0,00 (0,00)	0,00 (0,00)	1,000	H0 is accepted
Q8	1,36 (1,73)	1,15 (1,34)	0,551	H0 is accepted
Q9	0,94 (1,39)	0,68 (1,37)	0,512	H0 is accepted
Q10	3,00 (1,00)	3,68 (1,00)	0,018*	H0 is rejected

There was a significant difference in general satisfaction with sleep (Q10, $p<0.05$), with a higher score after applying the drug (3.68+1.00). The score related to the assessment of sleep quality (Q5) and hours of sleep (Q6) was also higher after applying the drug (Q5 = 3.73+0.87; Q6 = 3.36+1.01). This indicates improvement in self-assessment of sleep quality and reported hours of sleep. However, there was no significant difference ($p>0.05$).

Questions about waking up at night (Q4), difficulty staying awake during the day (Q8) and occurrence of pain and discomfort that interferes with sleep (Q9), values were higher before drug administration (Q4 = 2.05 + 1. 35; Q8 = 1.36 + 1.73; Q9 = 0.94 +1.39). This indicates that after administration of the drug the occurrences of these items were lower, which tends to improve sleep quality. However, there was no significant difference ($p>0.05$).

Table 5 presents the frequency (Questions 1 and 2) and average score before and after the responses of the “without formulation supplement” group.

Table 5. Comparison of before and after responses from the “on formulation supplement” group

		BEFORE	AFTER
Q1	BEFORE 20 h	0	0
	IN BETWEEN 20 - 21 h	0	1
	IN BETWEEN 21 - 22 h	0	0
	IN BETWEEN 22 - 23 h	2	8
	AFTER 23 h	15	8
Q2	BEFORE 5 h	0	0
	IN BETWEEN 5 - 6 h	7	4
	IN BETWEEN 6 - 7 h	7	8
	IN BETWEEN 7 - 8 h	1	2
	AFTER 8 h	2	3
Q3		2,64 (1,27)	3,94 (1,08)
Q4		2,47 (1,28)	1,17 (1,13)
Q5		2,47 (0,87)	3,58 (0,93)
Q6		2,23 (1,03)	3,41 (1,12)
Q7		0,64 (1,16)	0,35 (1,05)
Q8		2,35 (1,36)	0,82 (0,88)
Q9		0,94 (1,29)	0,52 (1,06)
Q10		2,29 (0,91)	3,64 (0,99)

The time at which individuals reported usually going to bed (Q1) fluctuated greatly after administration of the formulation supplement. The number of individuals who reported going to sleep between 10 and 11 pm rose from 2 to 8, while there was a drop in the option “after 11 pm” (7 people). These results indicate that more people started to sleep earlier. Regarding the time at which individuals reported waking up in the morning (Q2), there was an increase in the number of people who reported waking up between 6 and 7 am (1 person), 7 and 8 am (1 person) and after 8 am (1 person). This indicates that some people started to wake up later. Table 6 presents the before and after comparison of the responses of the “on formulation supplement” group using the Wilcoxon test.

Table 6. Wilcoxon test before and after responses from the “on formulation supplement” group

	BEFORE (Mean and standard deviation)	AFTER (Mean and standard deviation)	P-VALUE	CONCLUSION
Q3	2,64 (1,27)	3,94 (1,08)	0,001*	H0 is rejected
Q4	2,47 (1,28)	1,17 (1,13)	0,012*	H0 is rejected
Q5	2,47 (0,87)	3,58 (0,93)	0,001*	H0 is rejected
Q6	2,23 (1,03)	3,41 (1,12)	0,002*	H0 is rejected
Q7	0,64 (1,16)	0,35 (1,05)	0,102	H0 is accepted
Q8	2,35 (1,36)	0,82 (0,88)	0,001*	H0 is rejected
Q9	0,94 (1,29)	0,52 (1,06)	0,034*	H0 is rejected
Q10	2,29 (0,91)	3,64 (0,99)	0,001*	H0 is rejected

There is a significant difference in the time taken to fall asleep at night (Q3; p<0.05), night waking (Q4; p<0.05), self-assessment of sleep quality (Q5; p<0.05), hours of sleep per night (Q6; p<0.05), difficulty staying awake during the day (Q8; p<0.05), occurrence of pain and discomfort that interferes with sleep (Q9; p<0.05) and overall satisfaction with sleep (Q10, p<0.05).

The items time to fall asleep at night (Q3 = 3.94 +1.08)), self-assessment of sleep quality (Q5 = 3.58 +0.93), hours of sleep per night (Q6 = 3.41 +1 .12) and general satisfaction with sleep (Q10 = 3.64 +0.99) showed a higher score after drug administration, indicating a general improvement in sleep after drug administration.

The items night waking (Q4 = 1.17 +1.13), difficulty staying awake during the day (Q8 = 0.82 +0.88) and occurrence of pain or discomfort that interferes with sleep (Q9 = 0.52 +1.06) had a lower number of occurrences after sleep administration. Such values indicate a significant general improvement in sleep after administration of the drug. Table 7 presents the comparison of the “without formulation supplement” group with the “with formulation supplement” group in the period before formulation supplement administration using the Mann Whitney test.

Table 7. Mann Whitney test in the groups “with” and “without” formulation supplement in the period before formulation supplement administration.

	GROUP CONTROL (Mean and standard deviation)	GROUP WITH SUPPLEMENTATION (Mean and standard deviation)	P-VALUE	CONCLUSION
Q3	3,47 (0,96)	2,64 (1,27)	0,050	H0 is accepted
Q4	2,05 (1,35)	2,47 (1,28)	0,329	H0 is accepted
Q5	3,42 (0,83)	2,47 (0,87)	0,004*	H0 is rejected
Q6	3,05 (0,70)	2,23 (1,03)	0,005*	H0 is rejected
Q7	0,00 (0,00)	0,64 (1,16)	0,012*	H0 is accepted
Q8	1,36 (1,73)	2,35 (1,36)	0,053	H0 is accepted
Q9	0,94 (1,39)	0,94 (1,29)	0,889	H0 is accepted
Q10	3,00 (1,00)	2,29 (0,91)	0,037*	H0 is rejected

The group without formulation supplement (control group), in the period before the intervention, presented a significantly more positive score in the assessment of sleep quality (Q5; 3.47+0.96), hours of sleep per night (Q6; 3.05+0.70), difficulty breathing while sleeping (Q7; 0.00+0.00) and general satisfaction with sleep (Q10; 3.00+1.00) (p<0.05). Table 8 presents the comparison of the “without formulation supplement” group with the “with formulation supplement” group in the period after formulation supplement administration using the Mann Whitney test.

Table 8. Mann Whitney test in the groups “with” and “without” formulation supplement in the period before formulation supplement administration.

	GROUP CONTROL (Mean and standard deviation)	GROUP WITH SUPPLEMENTATION (Mean and standard deviation)	P-VALUE	CONCLUSION
Q3	3,36 (1,06)	3,94 (1,08)	0,119	H0 is accepted
Q4	1,94 (1,47)	1,17 (1,13)	0,132	H0 is accepted
Q5	3,73 (0,87)	3,58 (0,93)	0,666	H0 is accepted
Q6	3,36 (1,01)	3,41 (1,12)	0,908	H0 is accepted
Q7	0,00 (0,00)	0,35 (1,05)	0,129	H0 is accepted
Q8	1,15 (1,34)	0,82 (0,88)	0,597	H0 is accepted
Q9	0,68 (1,37)	0,52 (1,06)	0,952	H0 is accepted
Q10	3,68 (1,00)	3,64 (0,99)	0,920	H0 is accepted

There was no significant difference in any of the comparisons made ($p>0.05$). Table 7 showed superior sleep quality for the “without formulation supplement” group in the items sleep quality assessment (Q5; 3.47+0.96), hours of sleep in a night (Q6; 3.05+0.70), difficulty breathing while sleeping (Q7; 0.00+0.00) and general satisfaction with sleep (Q10; 3.00+1.00) ($p<0.05$). It appears that in the period after the intervention the “formulation supplement” group increased their scores on these items, which reduced the disparity between the two groups.

DISCUSSION

Analysis of Control Group Results Before and After Intervention: a) there was a significant improvement in overall sleep satisfaction (Q10) after formulation supplement administration, reflected in the higher score (3.68+1.00); b) sleep quality (Q5) and hours of sleep (Q6) also showed improvements after intervention, with higher scores (Q5 = 3.73+0.87; Q6 = 3.36+1.01); c) no significant differences were found in issues such as nighttime awakening (Q4), difficulty staying awake during the day (Q8), and occurrence of pain and discomfort interfering with sleep (Q9) after formulation supplement administration.

The analysis of "Formulation supplement" Group Results Before and After Intervention: a) Significant differences were found in several questions, including time to fall asleep at night (Q3), nighttime awakening (Q4), sleep quality (Q5), hours of sleep per night (Q6), difficulty staying awake during the day (Q8), occurrence of pain and discomfort interfering with sleep (Q9), and overall sleep satisfaction (Q10). All these items showed higher scores after formulation supplement administration, indicating significant improvements in sleep quality.

Comparison between Control and "Formulation supplement" Groups Before and After Intervention:

Before intervention, the no-formulation supplement group showed significantly more positive scores in some sleep-related aspects, such as sleep quality assessment (Q5), hours of sleep in one night (Q6), difficulty breathing while sleeping (Q7), and overall sleep satisfaction (Q10). However, after intervention, the formulation supplement group increased their scores in these questions, reducing the disparity between the two groups

The improvements in overall sleep satisfaction (Q10), sleep quality (Q5), and hours of sleep (Q6) observed in the control group align with findings from studies examining the placebo effect on sleep. For instance, another study [15] demonstrated that the expectation of receiving a treatment can influence subjective measures of sleep quality, even in the absence of active compounds. This effect may partially explain the modest improvements in these parameters within the control group. However, the persistence of challenges such as nighttime awakenings (Q4) and difficulty staying awake during the day (Q8) underscores the limited impact of psychological expectation on addressing physiological disruptions in sleep.

The significant improvements across all sleep-related parameters in the formulation supplement group corroborate findings from Ferracioli-Oda and coauthors [16], who highlighted the efficacy of melatonin precursors in enhancing sleep quality and reducing sleep onset latency. Additionally, related studies. [17] emphasized the potential of such interventions in regulating circadian rhythms and mitigating inflammation, which could explain the observed reductions in nighttime awakenings (Q4) and improved daytime alertness (Q8). These findings suggest that the formulation supplement not only improved subjective perceptions of sleep but also addressed underlying physiological factors contributing to sleep disturbances.

CONCLUSION

The results suggest that formulation supplement administration is associated with improvements in sleep quality, including reduced time to fall asleep, fewer nighttime awakenings, higher overall satisfaction, and improved sleep quality assessment. It is important to consider that, despite the observed improvements, some issues did not show significant differences, indicating areas where the formulation supplement may not have a direct impact. This discussion highlights the importance of formulation supplement intervention in improving sleep quality, but also underscores the need for broader and more in-depth studies to fully understand the impact and effects of formulation supplement on different aspects of sleep and overall health.

The limitations of this study include its relatively small sample size, which may limit the generalizability of the findings. Additionally, the reliance on self-reported questionnaires to assess sleep parameters introduces the potential for reporting bias. The study's short duration might not capture long-term effects of the intervention on sleep quality.

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