

Neo sleep ODT supplement – Dietary supplement in form of orally dispersible tablet containing highly soluble and bioavailable melatonin

Product advantages

- Neo sleep supplement contains an effective active ingredient combination combination of rapidly available melatonin for rapid sleep onset and selected active ingredients to improve sleep quality
- Due to the advanced formulation of **orally dispersible tablets (ODT)**, the product provides high administration comfort and ensures rapid release and absorption of melatonin. These properties are a strong prerequisite for high melatonin bioavailability and its full effect.
- With the help of an innovative approach, **at least 85% of the active substance melatonin from the tablet is released within 30 seconds, whereas** only 1-2% of this active substance is released in commercially available products at a comparable time. There has also been an **increase in cellular absorption of melatonin by more than 50% and an increase in its solubility by more than 100% compared to competing products.**
- The product also contains plant extracts standardized for **5-hydroxytryptophan, L-theanine, extract of magnolia standardized to magnolol, and B-complex**, which synergistically support the effects of melatonin, preventively contributing to good sleep and, moreover, against unwanted night-time awakening.
- U Neo sleep supplement, active substances are released and absorbed already in the oral cavity and the upper esophagus, avoiding the passage of the liver. This results in **multiple increased efficacy even at low doses. When active ingredients are administered in a classic tablet**, they pass through the gastrointestinal tract and subsequently the liver, where they are largely degraded or converted into ineffective substances - thus **reducing the effectiveness of the administered dose.**

Product description

- Based on **natural materials** - Neo sleep supplement contains only ingredients of natural origin
- **User-friendly form** – the minitab (4 mm diameter) dissolves in the mouth within 30 seconds without the need of drinking water
- Safe for long-term use, does not cause addiction and morning drowsiness
- Recommended dosage – 1 tablet to dissolve in the mouth just before bedtime
- Suitable for vegans and vegetarians

Scientific study (18th December 2017)

In the framework of research collaboration between mcePharma s.r.o. and First Faculty of Medicine, Charles University and its workplace Biotechnology and Biomedicine Center of the Academy of Sciences and Charles University in Vestec (Biocev), increased solubility and cellular absorption of melatonin as an active ingredient was achieved for the purpose of incorporation into the orally dispersible tablet (ODT) for rapid sleep onset.

Melatonin, the systematic name of which is 5-N-acetyltryptamine, is the hormone produced by the pineal gland (part of the mid-brain). This hormone plays an important role in controlling day and night rhythms. Melatonin levels in the body depend on the alternation of light and darkness, which is why its production is greatest during darkness, while during the day is blocked. Melatonin is attributed to the following effects:

- Suppression of subjective feeling of fatigue due to time shift ^{1 2}
- Reduction the time needed for falling asleep and lowering number of awakenings during the sleep cycle ^{3 4 5 6}
- Improves sleep quality ⁷

In order to promote the effect of melatonin on sleeping and quality of sleep, the active ingredients which contribute to the conditioning of the nervous system, psychological relaxation, as well as preventing anxiety (Table 1), have been included in the formulation.

Table 1: supportive active ingredients and their effect ^{9, 11, 12}

Active ingredient		Tablet content (mg)	Effect
Melatonin		3.0	Rapid sleep onset
5-hydroxytryptofan (5-HTP)		2.0	Serotonine supplies replenishment
L-theanine		2.0	Relaxation and anxiety prevention
Magnolol		1.0	Relaxation and anxiety prevention
B-complex	Vitamin B1	0.3	Conditioning of nervous system
	Vitamin B2	0.4	
	Vitamin B6	0.4	
	Vitamin B12	0.001	

In humans, 90% of oral melatonin is eliminated already during the first passage of the liver, which significantly reduces the effectiveness of the administered dose¹³.

Prevention of this undesirable phenomenon was achieved by a sophisticated procedure that involves the formation of the inclusion complex with melatonin already in the solid phase in combination with ODT. As a result, increased solubility of melatonin and its rapid release in the mouth is achieved, where most of it is absorbed. The aim of the experiments was to demonstrate rapid release of melatonin from the Neo sleep supplement and increased absorption of released melatonin in cell cultures compared to competing products A and B.

One of the problems associated with the use of melatonin is its insufficient solubility. This can be increased by the formation of complexes with a suitable substance. The formation of these complexes is governed by the stoichiometric ratios of the active substance, in our case melatonin, and complexing compounds. Upon subsequent contact with body fluid, active compounds are released from this complex. In the pharmaceutical industry, inclusion complexes and chelates are most often used. This procedure can also be used to solubilize melatonin as well.

The following parameters were studied in the study:

1. Comparison of melatonin release rate

Procedure: The aim of this experiment was to compare melatonin release from three products with equivalent melatonin dose (3 mg melatonin per tablet) by HPLC-MS (High Performance Liquid Chromatography) followed by mass spectrometry analysis.

Results: Neo sleep supplement releases at least 85% of the active ingredient melatonin after 30 seconds, whereas only 1-2% of melatonin is released from commercially available products. (Figure 4)

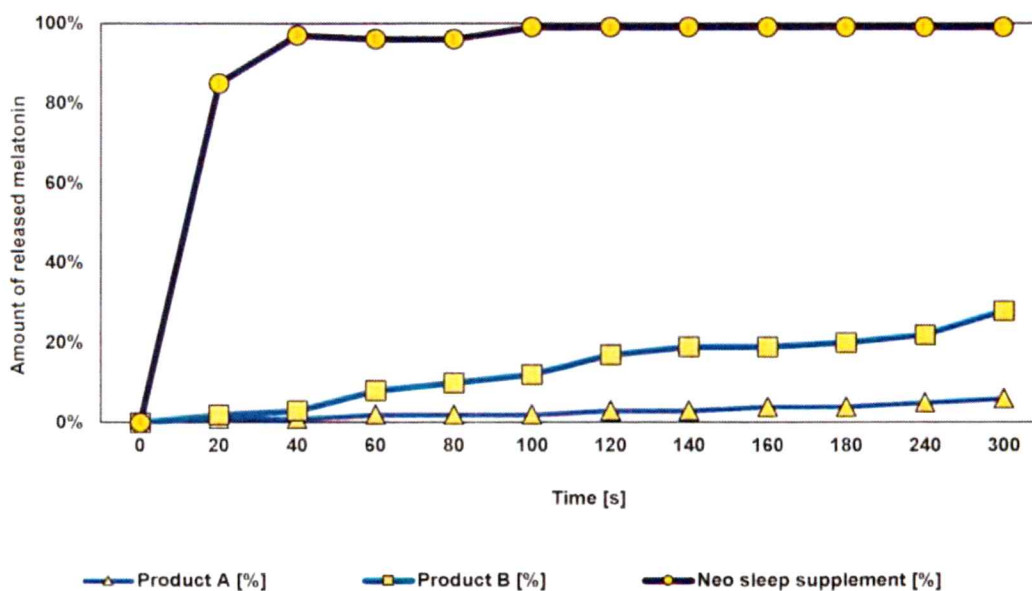


Figure 1: Relative percentage of melatonin released in solution, criterium = max. 3 mg melatonin / tablet. Neo sleep supplement releases at least 85% of melatonin within 30 seconds after administration.

2. Increased absorption into living cells of mouse breast carcinoma

Procedure: The aim of this experiment was to evaluate cellular absorption of melatonin in 3 competing products with equivalent melatonin concentration (3 mg melatonin per tablet). Within the experiment, the intensity of cell culture fluorescence was measured after 30 minutes of incubation with individual melatonin formulations. The fluorescence intensity is calculated from four points based on the intensity of the blue color in the object relative to the surrounding area.

Results: Fluorescence intensity of Neo sleep supplement (C) was found to be increased by more than 50%. (Figure 5 and 6), in comparison to competitive product samples A and B.

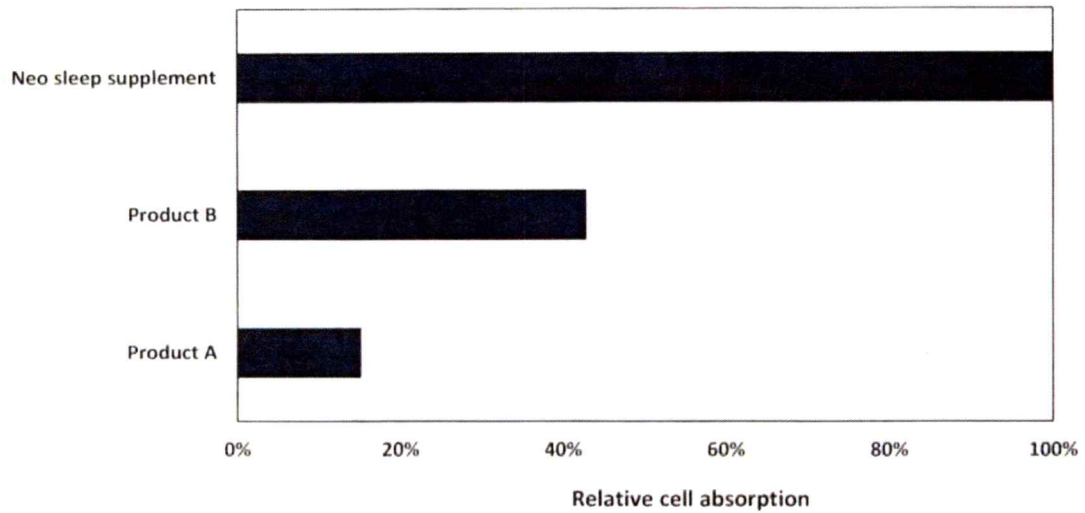


Figure 5: Comparison of relative cellular absorption in cell cultures of mouse breast cancer after incubation with competitive products A and B and Neo sleep supplement. Neo sleep supplement shows up to 50% increase in relative cellular absorption of melatonin compared to competitive products.

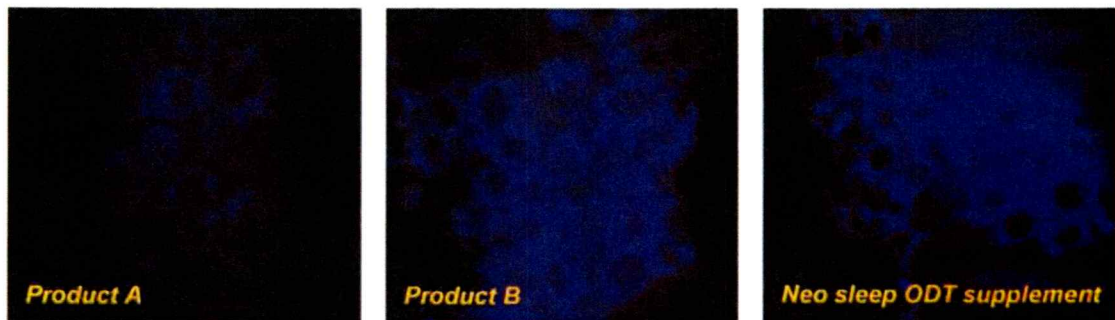


Figure 6: Images of cell cultures inoculated with competitive products A, B containing melatonin, and Neo sleep supplement. Melatonin from products A and B penetrates into cells to a much lesser extent. Melatonin from Neo sleep supplement is more absorbed by cells. (source: BIOCEV)

Conclusions:

- The Neo sleep supplement was developed within the framework of research and development collaboration between mcePharma s.r.o and the First Faculty of Medicine, Charles University and its Biotechnology and Biomedical Center of the Academy of Sciences and Charles University in Vestec (Biocev)
- Neo sleep supplement is an advanced product that contributes to rapid sleep onset, improves sleep quality, and promotes uninterrupted sleep
- Contains melatonin and synergistic 5-hydroxytryptophan, L-theanine, standardized magnolia extract and B-complex vitamins. They further contribute to the reduction of fatigue and exhaustion, to normal psychological activity and normal activity of the nervous system
- With an innovative approach, at least 85% of melatonin is released from the tablet within 30 seconds, while only 1-2% of this active substance is released in commercially available products in a comparable time.
- **An increase in cellular absorption of melatonin by more than 50% and an increase in its solubility by more than 100%** compared to classic products containing melatonin has also been achieved.
- The product is in the form of orodispersible tablets (ODT) providing administration comfort, rapid release and absorption of melatonin with increased cellular absorption. These properties are a strong prerequisite for high melatonin bioavailability and its full effect.
- In the case of Neo sleep supplement, the active ingredients are released and absorbed in the oral cavity and the upper esophagus, thereby avoiding the passage of the liver. They are therefore largely degraded or converted into ineffective substances. **This increases the effectiveness of the administered dose over competitive products.**

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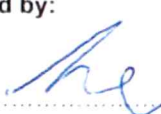
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