



Pinetonina™

Reduce stress and improve quality of sleep
the natural way

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Stress, anxiety and sleep disorders

Stress impacts many people around the world. The 2015 report entitled 'paying with our health' issued by the American Psychological Association estimated that over 70% of Americans regularly experience psychological and physical symptoms caused by stress. The majority also feels that their stress has increased over the past five years and that it has a negative impact on their personal and professional life.^{1,2}

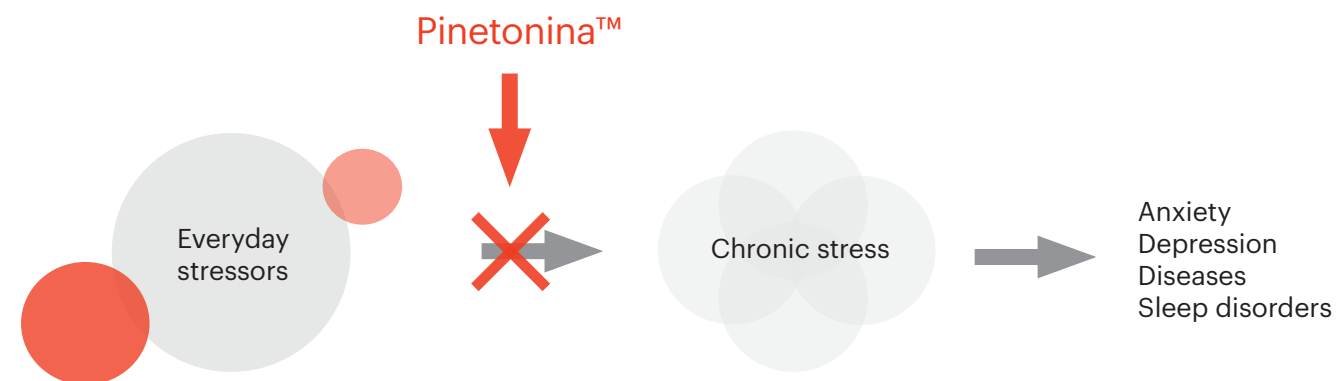
Everyday stressors most prevalent include job pressure, money, health, relationships, poor nutrition and sleep deprivation.^{3,4} Many times, these everyday stressors go unnoticed. When ignored, daily stressors can lead to chronic stress and in turn promote diseases like anxiety disorders, depression, high blood pressure, diabetes and heart disease.^{3,4} Current pharmacological treatment of stress and sleeping disorders has several side-effects including cognitive impairment, sexual dysfunction and sleep-disturbances.⁵ These adverse effects decrease patients' compliance to the therapeutic protocol.

Pinetonina™

Pinetonina™ is a natural, innovative nasal spray that combines the properties of lavender (*Lavandula Officinalis* and *Lavandula Dentata*) and fennel (*Foeniculum Vulgare*), both known for their anxiolytic and anti-stress activity. Lavender essential oil was found to be effective in improving quality of sleep without promoting sedative effects, relieving from symptoms of stress and anxiety and reducing levels of cortisol.⁶⁻¹⁷ Fennel has shown to decrease symptoms of anxiety, depression, stress and improve memory.¹⁸⁻²³

Before use, Pinetonina™ is diluted in physiological saline to prepare a 50% solution.

Pinetonina™ offers a natural alternative to existing pharmacological treatment, with the aim to reduce stress in an early stage and prevent it from becoming chronic. The active ingredients of Pinetonina™ are not known to cause sedative adverse effects, day somnolence, hang-over effect or drug abuse²⁴⁻²⁷ and can therefore be used as first-line therapy.



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The innovative nasal route of administration

The nasal mucosa is used as a route for the administration of many drugs. The non-keratinized and highly vascularized epithelium makes it a suitable route for the administration of both locally and systemically active drugs. Although direct evidence for nose-to-brain delivery in humans is still an emerging field of investigation, several studies indicate that nasal administration offers another promising delivery route.²⁸

By using the olfactory bulb, molecules are directly transported to the brain from the nasal cavity along the olfactory and trigeminal nerves, bypassing the blood-brain-barrier.^{28,29}

Advantages of nasal route of administration

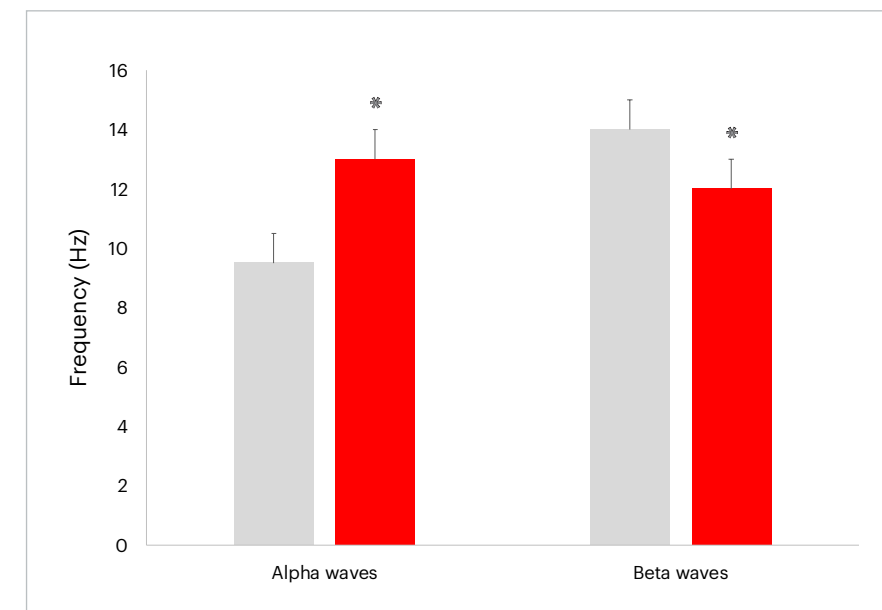
- Fast therapeutic effect
- Avoidance of hepatic first-pass effect
- Improvement of patient adherence
- Direct and fast transportation to the brain parenchyma

Safety and efficacy

When evaluated in vitro, Pinetonina™ was not considered cytotoxic.³⁰ In addition, systemic use of lavender and fennel are rendered to be safe for human use.^{8,18,31-32} Efficacy of Pinetonina™ was evaluated in two studies with 75 volunteers. Clinical parameters studied include electroencephalographs, salivary cortisol levels and quality of sleep.

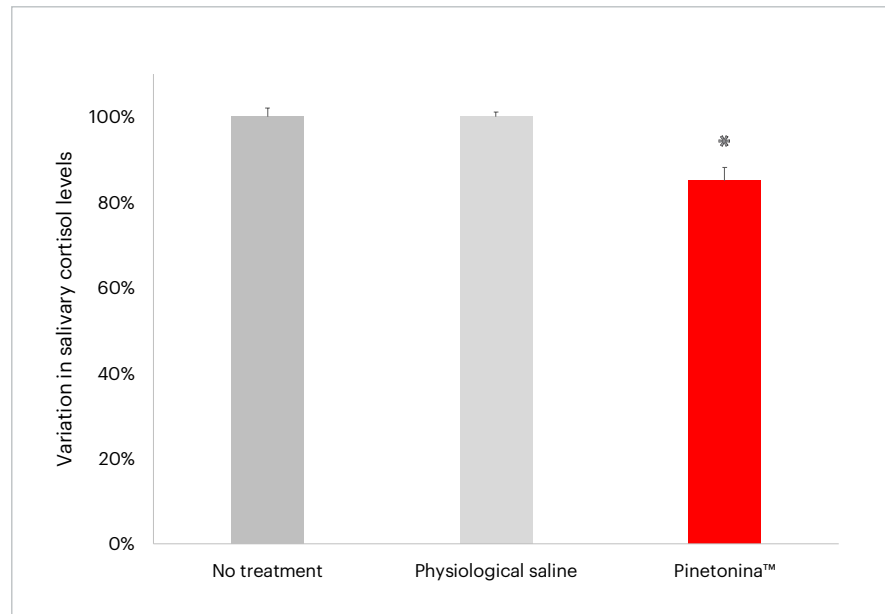
Electroencephalography

Frequency patterns of alpha and beta brainwaves were evaluated in volunteers receiving either two sprays of Pinetonina™ or two sprays of physiological saline solution 0.9% w/v in each nostril, twice daily. Thirty minutes after administration of Pinetonina™, the electroencephalogram showed a significant increase and decrease in alpha and beta brainwaves respectively.³⁰



Frequency of brain waves after administration of Pinetonina™ (red) or physiological saline solution 0.9% (gray). Differences were significant ($P < 0.05$).

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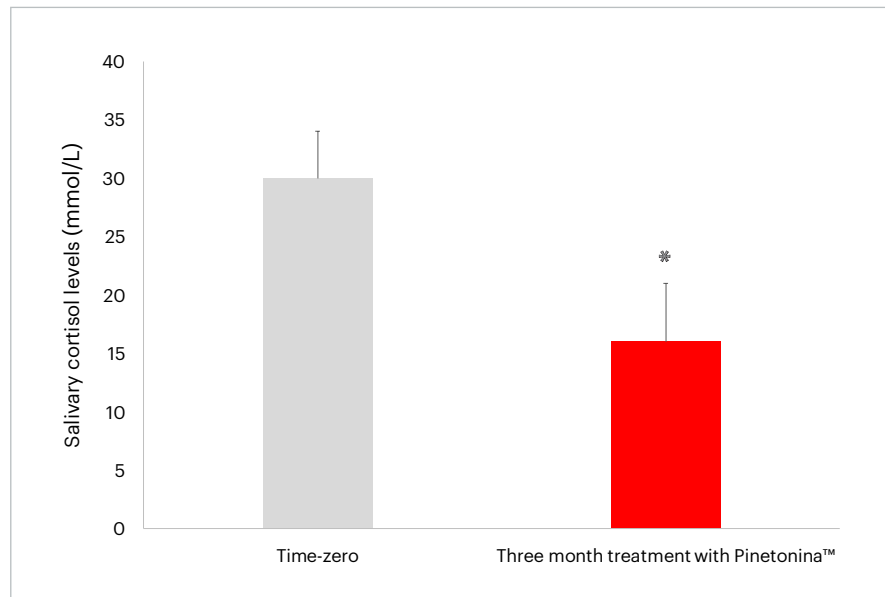


After 15 days of Pinetionina™, salivary cortisol levels were significantly lower compared to the other two groups (P < 0.05).

Salivary cortisol levels

Salivary cortisol was evaluated in two different studies. In the first, volunteers received either two sprays of Pinetionina™ or two sprays of physiological saline solution 0.9% w/v in each nostril, two times daily for 15 days. The control group received no intranasal application.³⁰ In the second study, one application of the Pinetionina™ per nostril was administered once a day. Salivary cortisol levels were obtained at time-zero and after 3 months. Volunteers served as their own control.³³

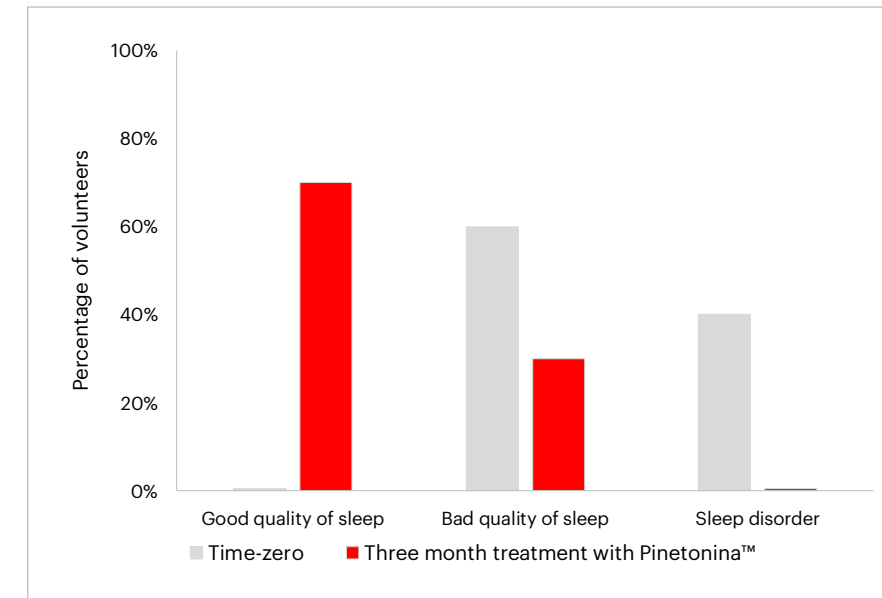
In the first study, the group treated with Pinetionina™ showed significant reduction of salivary cortisol levels compared to the group receiving no intranasal application and the group receiving the physiological saline after 15 days.³⁰ In the second study, the reduction of salivary cortisol levels with Pinetionina™ were shown to be long-lasting; total levels of cortisol were still significantly decreased after 3 months of use.³³



Levels of salivary cortisol in volunteers using daily Pinetionina™ were significantly reduced after 3 months (P < 0.05).



Suggested formulations Reduce stress and improve quality of sleep



Pittsburgh Sleep Quality Index (PSQI) in patients who used Pinetionina™ 50% for 3 months

Quality of sleep

Quality of sleep was evaluated through the validated Pittsburgh Sleep Quality Index (PSQI), a self-rated questionnaire which assesses sleep quality and disturbances. With Pinetionina™, a statistically significant difference was observed after 3 months of use, compared to the control group.³³

Pinetionina™ - summary of activity

- Increases** alpha brainwaves frequency, related to relaxation, visualization and creativity.
- Decreases** the frequency of beta brainwaves that are related to alertness.
- Increases** quality of sleep.
- Reduces** salivary cortisol, a stress related hormone.

Prevent stress from becoming chronic; use Pinetionina™ as a natural, non-addictive first-line treatment. For more information on Pinetionina™, please contact your local sales representative.

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