



### Index

- Key figures and traditional use
- Affron® values
- Strong scientific evidences
- Local sourcing, Patented technology, High-Quality standards
- Summary







**Key figures and traditional uses** 





# **Stress is a major concern**

"Stress can be defined as a general sensation of overwhelming and unability to cope with pressures in our lives<sup>1</sup>"

#### Causes of **stress**<sup>1</sup>:

- Health concerns
- Life financial problems •
- Job pressure

- Demands of fast living
  - **Sleep deprivation**

Stress is the cause of **50-60%** of the absenteeism at workplace<sup>2</sup>

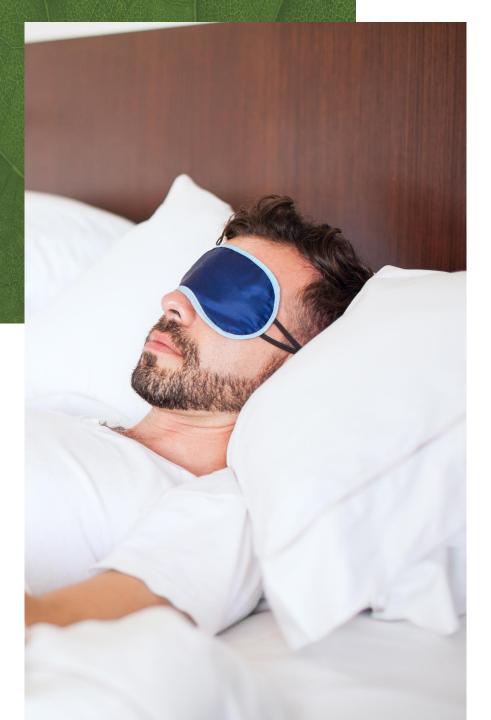




# **Are young people stressed?**

- Teenagers are some of the most vulnerable targets for stress, and their parents are seeking natural, and holistic solutions to help them feel more positive<sup>1</sup>.
- **37%** of **competitive gamers** in the US have consumed food/drink products with relaxing benefits<sup>2-3</sup>.





# Who suffers from sleep disorders?

**10-15%** of the adult population has insomnia<sup>1</sup>

**25-35%** due to stressful situations<sup>1</sup>

# How does sleeplessness affect cognitive performance?

**Sleep deprivation** has been linked to higher index of obesity, distress and negative moods<sup>3</sup>.

Getting **5 hours** or less of sleep for 4 nights

=

Blood alcohol content (BAC) of 0.6 (3 drinks)<sup>2</sup>



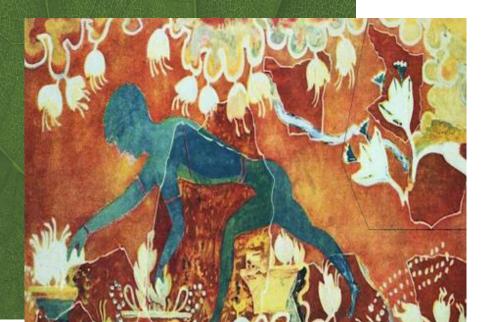




Affron® values



**\*+4 million** people worldwide benefit from affron® to maintain a positive mood, improve occasional stress, and sleeplessness, every day<sup>1</sup>"







## The best known ancient spice

- Saffrons' history of use goes back to the ancient times, being mentioned by authors like Solomon and Homer<sup>1</sup>.
- The oldest reference to saffron harvesting was found on a fresco of the Minos Palace in Crete (1600-1700 BC)<sup>1</sup>.
- Traditionally, it has been used as a sedative, expectorant, and adaptogenic agent<sup>2</sup>.

## Pharmactive proud adopter of saffron

#### **American Botanical Council**

Pharmactive is a reference for saffron extracts in the market thanks to our extensive knowledge of saffron.



(1) ES2573542B1; (2) WO2017182688A1.





## **Bioactive compounds**

- Affron® (Crocus sativus L.) is standardized to Lepticrosalides®
   3.5% by HPLC.
- Lepticrosalides® is a patented totum of bioactive compounds that has been shown in 9 clinical studies to act synergistically and be responsible of the effectiveness of saffron against low mood, anxiety, and insomnia at different stages of life<sup>1-8</sup>.

# **Award-Winning Ingredient**

**NutraIngredients USA Awards 2020** 

INGREDIENT OF THE YEAR

**Cognitive Function** 

**NutraIngredients EUROPE Awards 2022** 

INGREDIENT OF THE YEAR

**Healthy Ageing** 



### Most awarded saffron extract worldwide

#### **Frost & Sullivan**



#### NutraIngredients Award



### What leading experts say



technology platform (AFF®ON Cool-Tech)

#### **NIE Awards Winner**



#### **Innovation Awards**



Frost & Sullivan Award 2021



# **Unlock your potential with affron®**

9 human clinical studies published<sup>1-9</sup>

Unique with 2 dose-response studies<sup>1,8</sup>

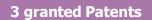
Clinically studied in adolescents3

Most clinically validated saffron extract

**Rapid absorption** in 1 hour<sup>10</sup>

Most awarded saffron extract





**Environmentally** responsible: patented green extraction technology AFF® ON Cool-Tech11 & Locally Sourced (own saffron fields)

> **Made in Spain DNA** certified

**Proven bioavailability** (pharmacokinetics study)10

Lowest dosage: 14 mg x 2/day





























### **Galenic formulations**

Unique Water-soluble. Multiple applications.

Accurate for food matrices.



# **Recommended daily dose**

#### 14 mg x 2/day:

- Mood improvement.
- Stress.
- Menopause symptoms.
- Master sleep.

### **Botanical info**

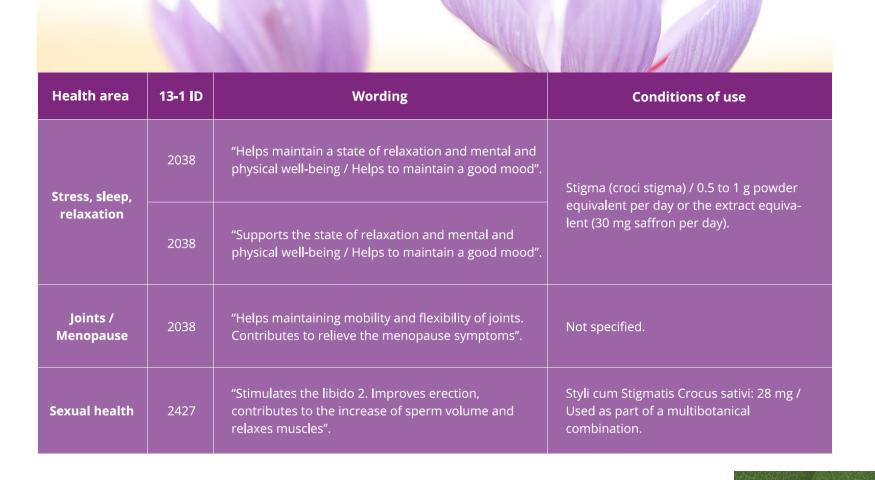
- Botanical name: Crocus sativus L.
- Family: Iridaceae.
- Common name: Saffron.
- Part of the plant: Stigma.

### Other info

- Shelf life: Three years\*.
- Non-GMO. Non-Irradiated.
- MOQ: 1 Kg.



# **Europe: EFSA on-hold claims**





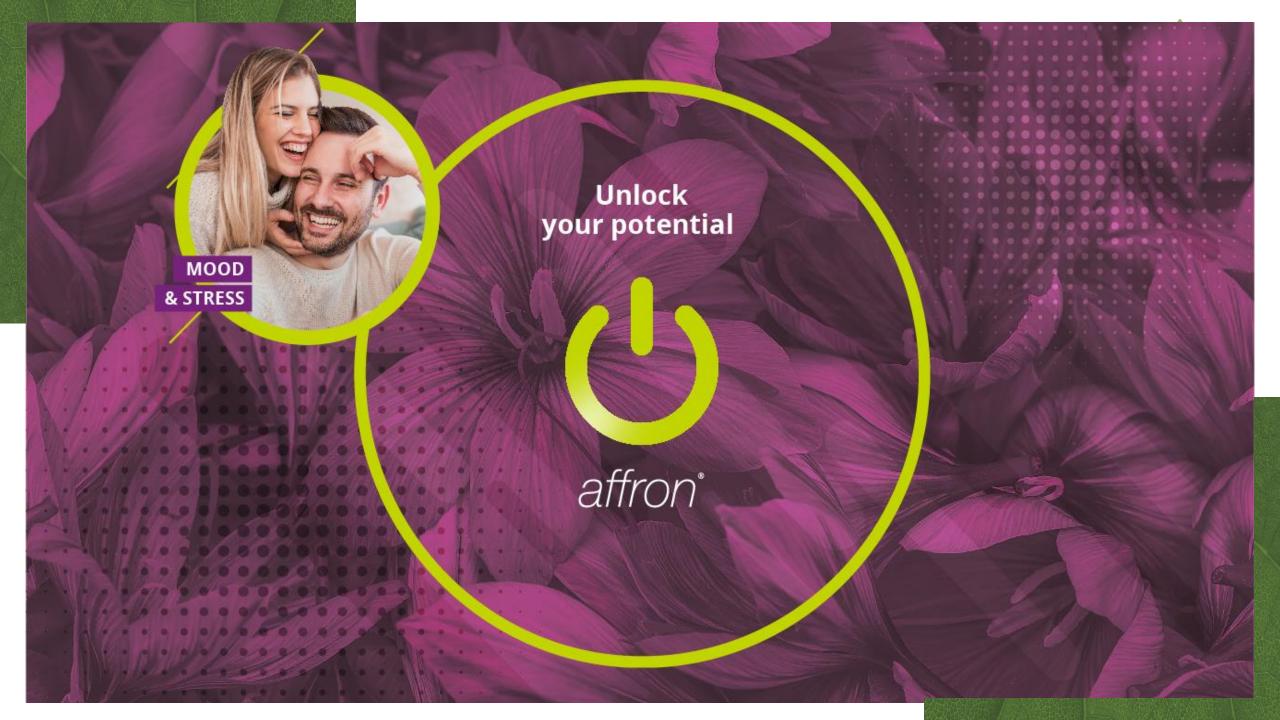


Strong scientific evidence



# 9 Human clinical studies published and pharmacokinetics

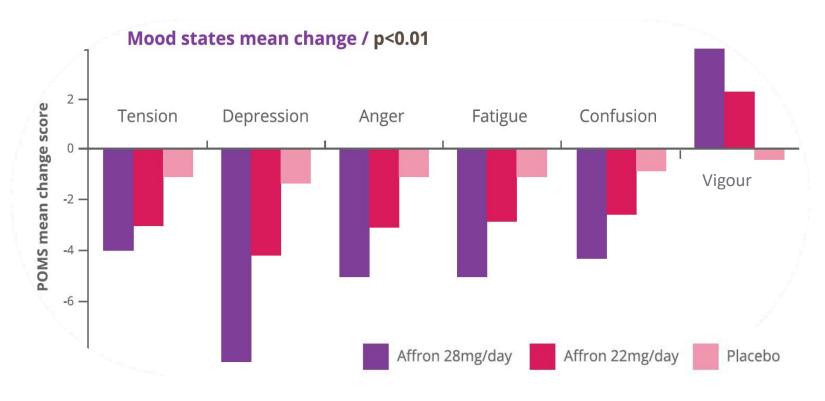
Study Reference	Evidence field	Design	
Kell G., et al. <i>ComplementaryTherapies Medicine</i> 2017 Aug; 33:58-64	Improve mood, occasional stress, tension, and associated anxieties	Randomized, double-blind, placebo-controlled study. Dose-response.	
Lopresti AL, et al. <i>J Psychopharmacol</i> . 2019 33:1415-1427			
Lopresti AL, et al. <i>J Affect Disord</i> . 2017 Jan 1;207:188-196		+740 parti	
Lopresti AL., et al. <i>J Affect Disord</i> . 2018 May; 232:349-357	Mood improvement and associated anxieties in adolescents	Randomized, double-blind, placebo-controlled study.	
Nishide, A, et al. <i>Japanese Pharmacology and Therapeutics</i> . 2018 (8); 46:1407-1415			
Lopresti AL, et al. <i>J Clin Sleep Me</i> d. 2020	Improve occasional sleeplessness		
Lopresti AL, et al. Sleep Medicine 86 (2021) 7-18		Randomized, double-blind, placebo-controlled study. Dose-response.	
Lopresti AL, et al. <i>Journal of Menopausal Medicine</i> . 2021;27:1-13	Mood improvement in menopausal women	Dandardinad dauble blind pleashs controlled to the	
Lopresti AL, et al. Journal of the International Society of Sports Nutrition 19:1, 219-238,	Mental and physical effects of affron® during sports activities.	Randomized, double-blind, placebo-controlled study.	
Almodovar P., et al. <i>Evidence-Based Complementary and</i> Alternative Medicine 2020	Pharmacokinetics	PHARMACOKINETIC STUDY: A single dose, randomized, double blinded study.	





# **Affron® improving mood**

In a randomized, double-blind, placebo-controlled study (N=128) **affron® intake of 28mg/day** for 4 weeks, significantly **improved mood disorders, such as tension, anger, depression, fatigue and confusion. Affron®** intake was **well tolerated and no side effects were associated**.





# **Affron® improving mood**

In a randomized, double-blind, placebo-controlled study **affron**® **intake of 28mg/day** for 4 weeks, significantly **improved mood disorders, such as tension, anger, depression, fatigue and confusion, being well-tolerated.** 

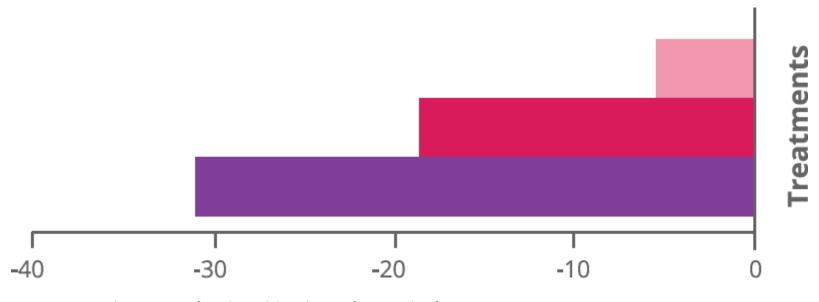


Figure: Mean change score of total mood disturbance after 4 weeks of treatment.





### **Affron® evidence in adolescents**

#### The unique saffron extract tested on adolescents.

In a randomised, double-blind, placebo-controlled study (N=68), the administration of **affron**® for **8** weeks improved anxiety and depressive symptoms in adolescents (12-16 years old) with mild-to-moderate symptoms, from the perspective of the adolescent.

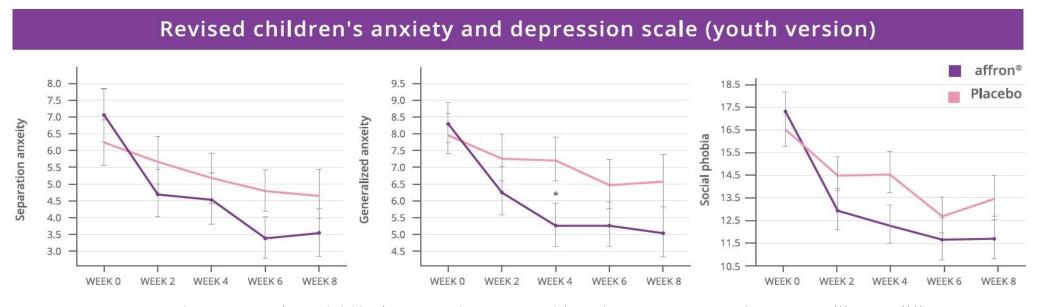


Figure: Change in RCADS (Revised Children's Anxiety and Depression Scale). Youth raw scores over 8-week intervention. (\*)p <0.05; (\*\*)p <0.01



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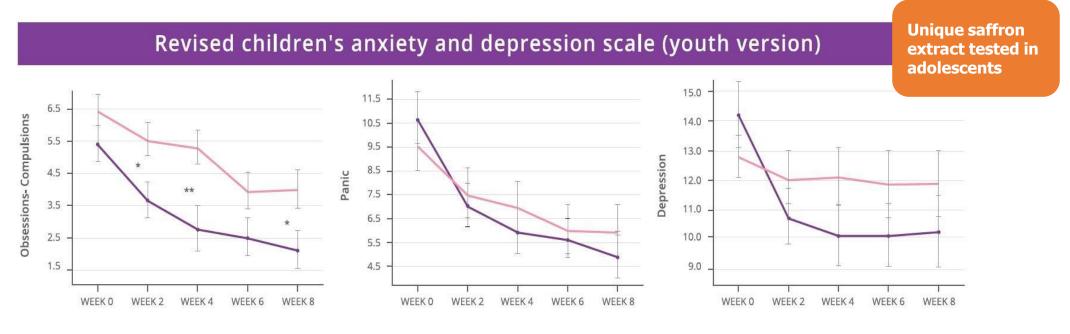


Figure: Change in RCADS (Revised Children's Anxiety and Depression Scale). Youth raw scores over 8-week intervention. (\*)p <0.05; (\*\*)p <0.01

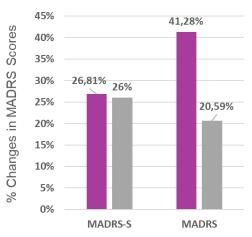


# **Affron®** in coadjutant treatment with antidepressants

In a randomised, double-blind, placebo-controlled study (N=68), the administration of **affron**® for **8 weeks** was associated with reduced side effects associated with antidepressant intake and increased antidepressant effects in adults currently taking pharmaceutical antidepressants.

#### Reduction in the depression rating scale MADRS

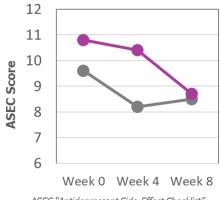
Percentage of reduction in self-report MADRS-S and clinician-rated MADRS over 8-week intervention



MADRS "Clinician-rated Montgomery-Asberg Depression Rating Scale "MADRS-S" Self-rated MADRS"

#### Reduction in antidepressant sideeffects (ASEC)

Reduction in ASEC over time 12

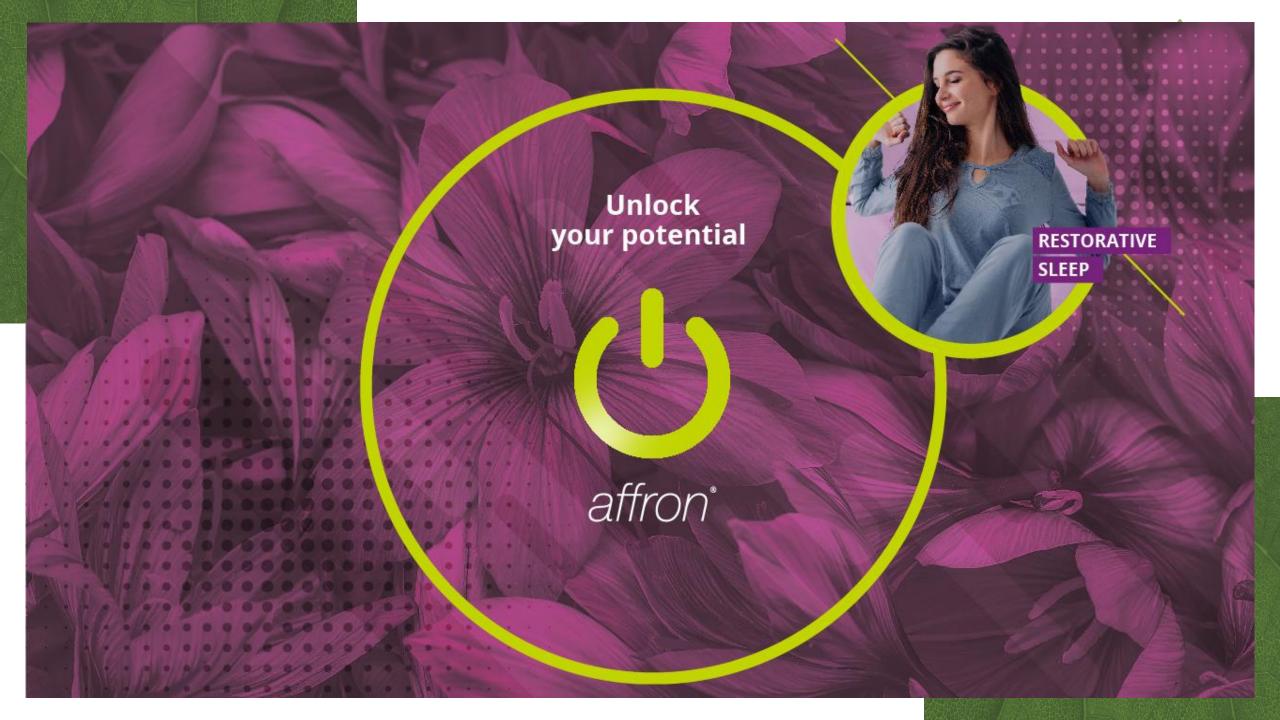


ASEC "Antidepressant Side-Effect Checklist"

#### **Consumer Satisfaction Ratings**

**71%** of participants continued taking affron® after the study

**73%** of participants were satisfied with the affron® consumption

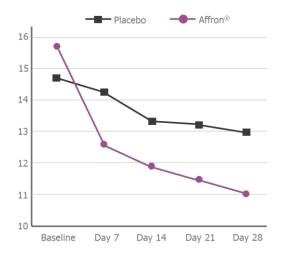




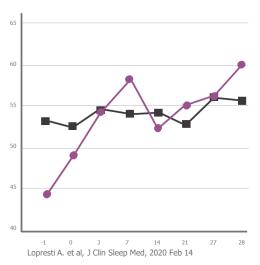
# **Affron® improving occasional insomnia**

- Affron® intake for 28 days was associated with greater improvements in:
  - **Sleep quality** as measured by the ISI, with most changes occurring in the first 7 days of treatment.
  - Restorative sleep as measured by the RSQ.
  - Sleep quality and strong trend suggesting greater reductions in the number of awakenings after sleep onset and increases in alertness upon awakening.
- Affron® intake was well tolerated and no side effects were associated.
  - 96% of participants in the affron® group were satisfied with their tablet intake.

#### **Insomnia Severity Index Score (ISI)**



#### **Restorative Sleep Questionnarie Score (RSQ)**



#### New!



# **Study Design**

**Design:** Three-arm, parallel-group, randomised, double-blind, placebo-controlled trial.

**Objective:** To validate and extend on previous positive findings of the sleep-enhancing effects of affron<sup>®</sup> in adults with unsatisfactory sleep.

**Dosage:** 14 / 28 mg of affron® / placebo 1 hour before sleep.

Participants: 120 healthy adults, aged 18 to 70, with self-reported sleep

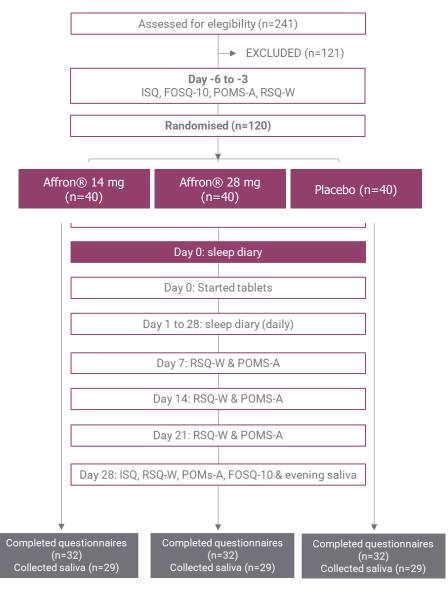
problems for over 4 weeks.

**Study duration:** 28 days.

**Impact factor:** 3.492(Q1).

#### **Outcomes measures**

- Pittsburgh Sleep Diary (PSD).
- Profile of Moods states Abbreviated Version (POMS-A).
- Insomnia Symptom Questionnaire (ISQ).
- Restorative Sleep Questionnaire Weekly Version (RSQ-W).
- Functional Outcomes of Sleep Questionnaire (FOSQ-10).
- Salivary cortisol and melatonin (evening).





## Affron® improved sleep quality even a low dose

A single dose of affron® 1 hour before sleep for 4 weeks showed a significant improvement of **24.6%** of sleep quality compared to placebo (p<0.001).

# Sleep Quality improvements after 4 weeks (PSD)

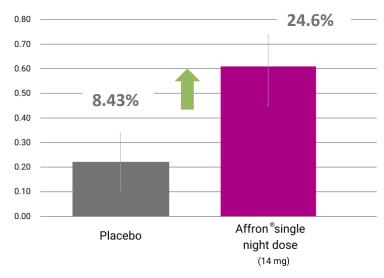


Figure 1. Changes in sleep quality ratings from baseline to week 4

By the very first time, a single dose of affron<sup>®</sup> 1 hour before sleep revealed an increase in melatonin concentration from baseline to week 4 compared to the placebo (p=0.036).

#### Change in evening Melatonin (pg/ml)

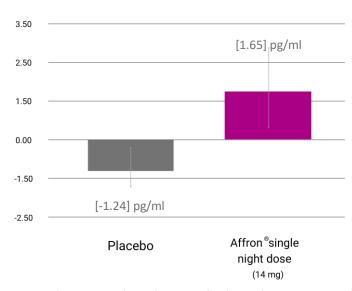
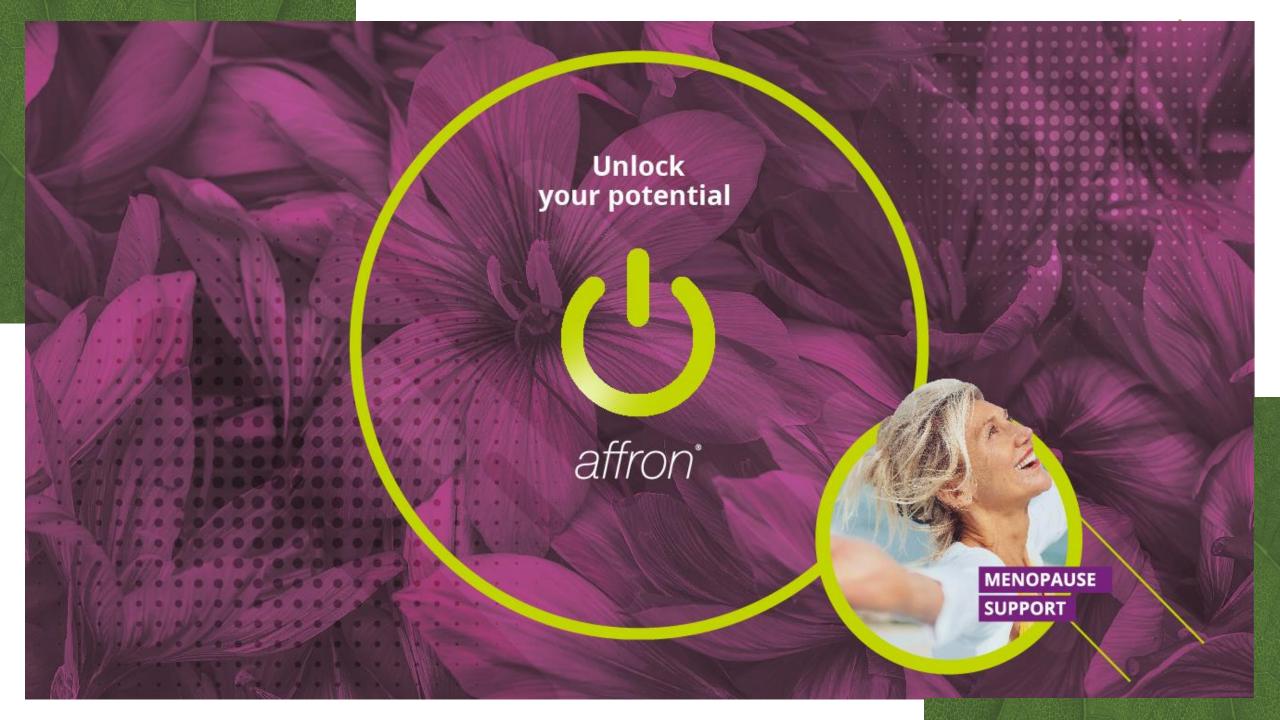


Figure 2. Changes in salivary hormone (melatonin) concentrations from baseline to week 4.

Lopresti AL, et al. Sleep Medicine 86. 2021;7-18





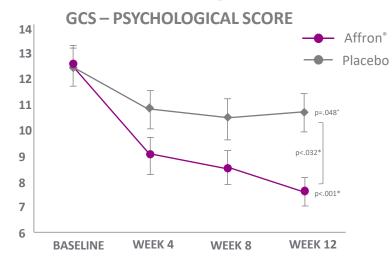
# Affron® improved mood on menopausal women with no estrogenic effect

In a randomized, double-blind, placebo-controlled study (N=128) **affron**® **intake of 28mg/day for 12 weeks, significantly improved the psychological aspects** of the Greene Climacteric Scale (GCS), characterized by:

- 33% reduction in anxiety symptoms
- 32% reduction in depression symptoms

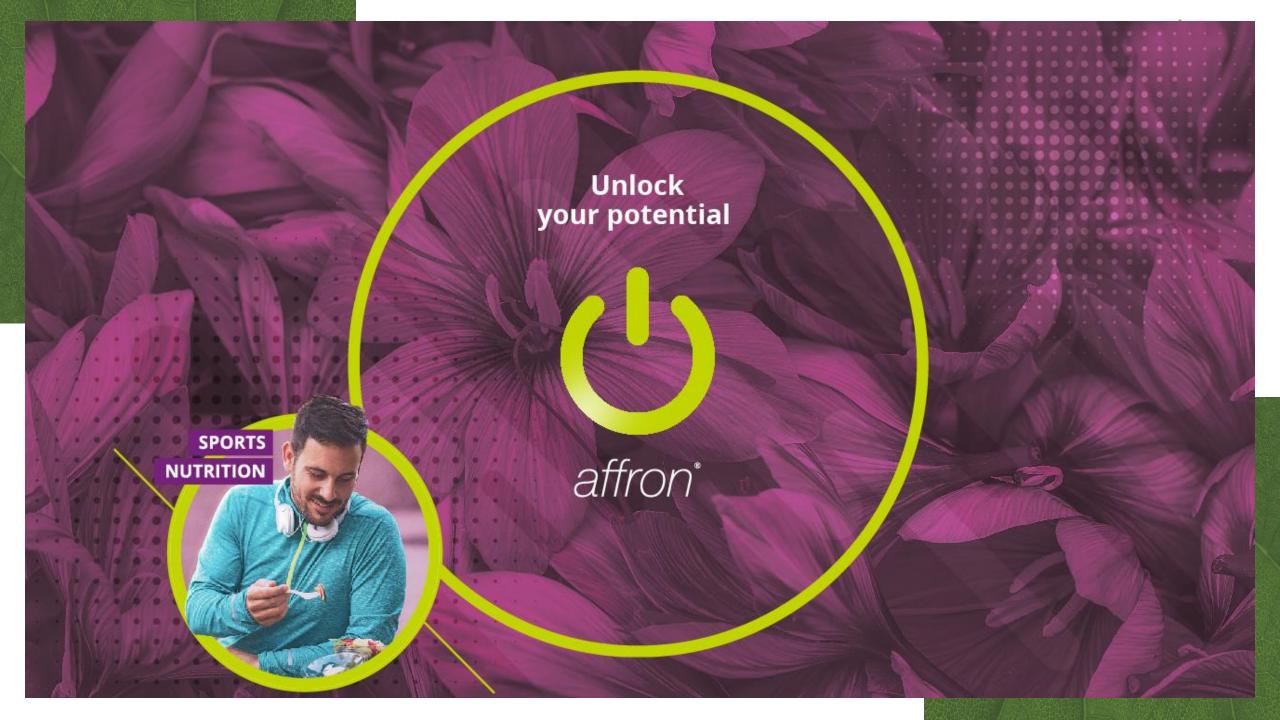
#### No undesirable estrogenic effects were reported.

Unique saffron extract tested for menopausal symptoms

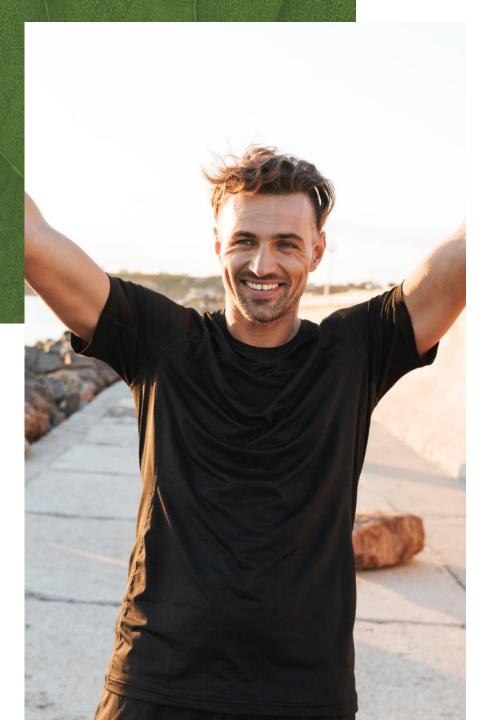


#### **PSYCHOLOGICAL SYMPTOMS**

- 1. Heart Beating quickly or strongly
- 2. Feeling tense or nervous
- 3. Difficulty in sleeping
- 4. Excitable
- 5. Attacks of anxiety, panic
- 6. Difficulty in concentrating
- 7. Feeling tired or lacking in energy
- 8. Loss of interest in most things
- 9. Feeling unhappy or depressed
- 10. Crying spells
- 11. Irritability







## Pleasure and enjoyment during sports activities

Feelings of pleasure and enjoyment associated with exercise are positively associated with exercise adherence<sup>1-2</sup>.

Strategies to improve recovery after exercise may encourage greater exercise adherence, increase overall pleasure associated with exercise, enhance the mental and physical benefits derived from regular physical activity, reduce the risk of physical injury, and improve overall performance<sup>3-5</sup>.

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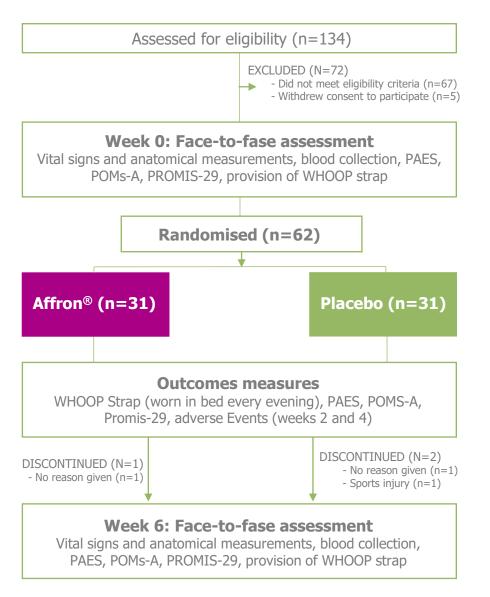
# **Study summary**

#### **STUDY FEATURES**

- **Design:** Randomized, double-blind, placebo-controlled study.
- **Objective:** The aim of this study was to investigate the effects of affron® supplementation in recreationally adults on mood, exercise enjoyment and recovery.
- **Participants:** 62 adults engaging in regular exercise.
- **Dosage:** affron® 14mg twice daily or a placebo.
- Study duration: 6 Weeks.

#### **OUTCOME MEASURE**

- Physical Activity Enjoyment Scale (PAES).
- Profile of Mood States (POMS-A).
- Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29).
- WHOOP strap: to measure changes in sleep quality, resting heart rate, and heart rate variability.





# Affron® improved enjoyment in active adults

In this 6-week, randomized, double-blind, placebocontrolled trial, supplementation with 14 mg, twice daily of a saffron extract (affron®) in recreationally active adults was associated with improvements in selfreported **exercise enjoyment and mood.** 

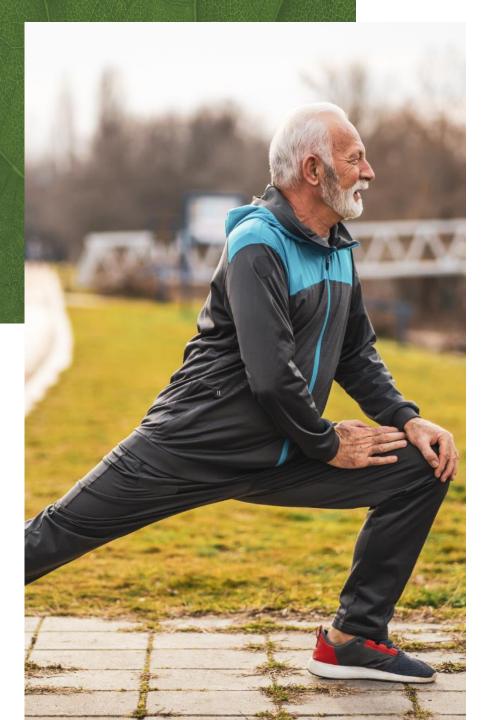


# Affron® improved enjoyment in active male adults

When changes in exercise enjoyment were analyzed by sex, there was a **significantly greater** improvement in males taking affron® compared to the placebo.







# **Affron®** may increase parasympathetic activity

Changes in resting heart rate (RHR) and heart rate variability (HRV) are indicators of recovery as studies have demonstrated that compared to healthy controls, adults with stress and/or burnout have an elevated RHR and decreased HRV.



Figure 2. WHOOP strap

Males have statistically significantly large increase in HVR over time in the affron® group compared to the placebo group (p = 0.001). Comparing baseline to week 6 there was a statistically significant decrease (5.74%) in the placebo group (p = 0.029).

Results suggested that affron® may increase parasympathetic activity in males but not females.



### A move towards the MAINSTREAM

80% of consumer have tried sports nutrition in the last 6 months<sup>1</sup>

of consumer said "natural" is the most importan claim in sports nutrition<sup>1</sup>

**Sports nutrition** is **now more inclusive than ever**, offering nutrition (product) solutions for all consumers no matter who they are, what they do, or when they want it.

The **primary trends** that underpin growth include convenience, **plant-based ingredients** and a **greater focus on benefits related to everyday** 'performance'.





# Recovery and sleep

Sleep is essential for the brain and the body and is dependent on the quality of the sleep cycle. We need at least 7-10 hours of sleep a night to function optimally<sup>1</sup>.

Poor quality sleep over a long period of time could reduce athletic performance.

A lack of sleep or quality of sleep can negatively affect mood, learning, memory, cognition, pain perception, immunity, and inflammation<sup>1</sup>.

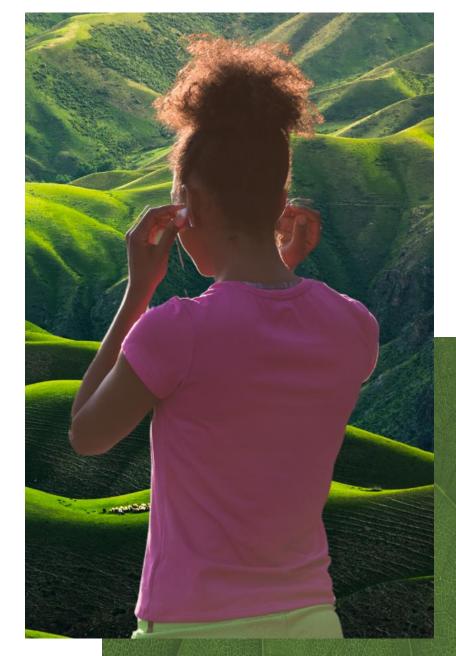
# Performance, recovery and sleep

Athletes of all standards continue to seek any advantage that may improve their performance.

Recovery aims to restore physiological and psychological processes to achieve the optimum level.

Two of the most popular interventions are nutrition and sleep.

Sleep is the fourth stage of performance. To prepare, perform, recover, and sleep.





### PREMIUM OVERNIGHT PROTEIN

Developed by sleep experts, our overnight protein combines the nourishing power of plant protein with 28mg **affron**® to **promote sleep by helping you to relax and feel good**. With soothing flavours, overnight regeneration has never tasted so good.

- **❖ 15-20g plant-based protein | high in aminoacids**
- **♦ Affron®** | aids restful sleep
- Creamy and soothing flavours
- 100% natural and plant based



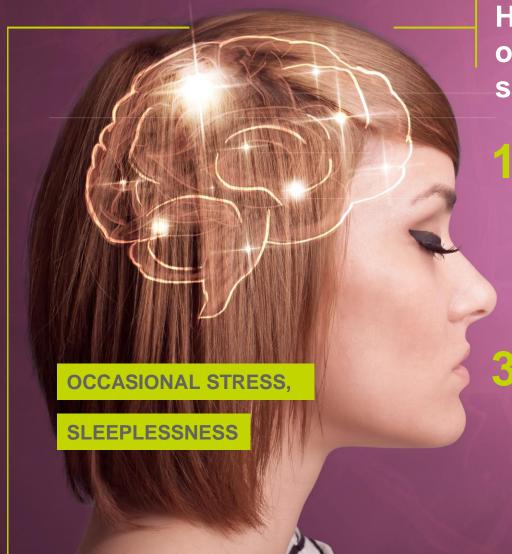
#### **Suggested EFSA Claims**

BOTANICAL INGREDIENT	WORDING	RECOMMENDED DOSAGE
Saffron	Helps maintain a state of relaxation and mental physical well-being.	30 mg
Plant-based protein	Protein contributes to the maintenance of muscle mass.	15 g _









# How your brain reacts against occasional stress and sleeplessness?

# Increases the inflammatory response

- Inflammatory markers (IL-1β, TNFα).1
- ✓ Anti-inflammatory marker (IL-10) .²
- Cortisol release.1-.
- ▼ Decreases selective serotonin and dopamine reuptake inhibitor response.¹-²
- ✓ Decreases serotonin and dopamine levels.¹-²

#### **Oxidative stress**

- Increases ROS (Reactive Oxygen species).5
- Increases de neuronal damage.5

# Decreases the neurotransmitter balance

- Increases reuptake of major neurotransmitters such as norepinephrine, serotonin, adrenaline.3-4
- Increases enzymatic breakdown of dopamine, norepinephrine and serotonin.<sup>3-4</sup>

# Decreases Neuronal Plasticity

- Reduces BDNF expression.<sup>6</sup>
  (Molecule involved in neuronal plasticity and connectivity processes).<sup>6</sup>
- Reduces the cognitive capacity and neuronal recovery of mood.<sup>6</sup>

1. Zhang, C. et al. "Neuroprotective effects of safranal in a rat model of traumatic injury to the spinal cord by anti-apoptotic, anti-inflammatory and edema-attenuating." Tissue and Cell 47.3 (2015): 291-300.; 2. Baluchnejadmojarad, T. et al. "Safranal, an active ingredient of saffron, attenuates cognitive deficits in amyloid β-induced rat model of Alzheimer's disease: underlying mechanisms." Metabolic brain disease 34.6 (2019): 1747-1759.; 3. Hosseinzadeh H. Et al., Anxiolytic and hypnotic effect of Crocus sativus aqueous extract and its constituents, crocin and safranal, in mice". Phytother Res. (2009) Jun;23(6):768-74; 4. Georgiadou, G et al. "Effects of the active constituents of Crocus Sativus L., crocins, in an animal model of obsessive-compulsive disorder." Neuroscience letters vol. 528, 1 (2012): 27-30; 5. Ahmad, Abdullah Shafique, et al. "Neuroprotection by crocetin in a hemi-parkinsonian rat model." Pharmacology Biochemistry and Behavior 81.4 (2005): 805-813.; 6. Ghasemi, T., et al. "Antidepressant effect of Crocus sativus aqueous extract and its effect on CREB, BDNF, and VGF transcript and protein levels in rat hippocampus." Drug research 65.07 (2015): 337-343.

## How affron® can help you?

# Decreases the inflammatory response

- Inflammatory markers (IL-1β, TNFα).<sup>1-2</sup>
- Anti-inflammatory marker (IL-10) .1-2
- ✓ Cortisol release.¹-²
- Increases selective serotonin and dopamine reuptake inhibitor response. 1-2
- Increases serotonin and dopamine levels.1-2

# Decreases oxidative stress

- Decreases ROS (Reactive Oxygen species).5
- Increases de activity of the antioxidant enzymes GPx, GSR, catalase and SOD.<sup>5</sup>

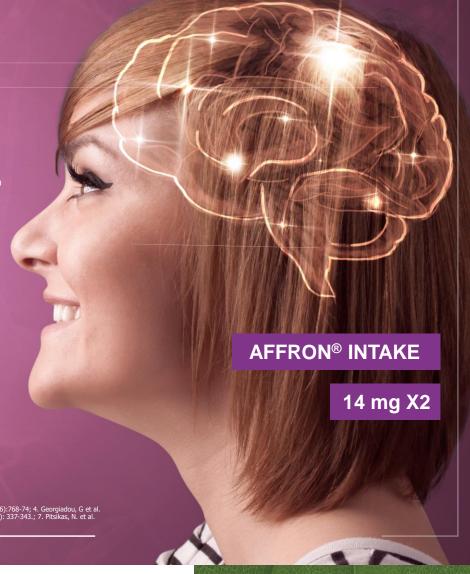
  Delay the celular ageing and promote cognitive improvement.<sup>5</sup>

# Increases the neurotransmitter balance

- ✓ Decreases euptake of major neurotransmitters such as norepinephrine, serotonin, adrenaline <sup>3-4</sup>
- Decreases enzymatic breakdown of dopamine, norepinephrine and serotonin and maintain the correct level of acetycholine.<sup>3-4</sup>
- △ Increase GABAergic response to induce sleep.<sup>7-8</sup>

# Increases Neuronal Plasticity

- Increases BDNF expression.<sup>6</sup>
  (Molecule involved in neuronal plasticity and connectivity processes).
- Increases the cognitive capacity and neuronal recovery of mood.<sup>6</sup>



1. Zhang, C. et al. Tissue and Cell 47.3 (2015): 291-300; 2. Baluchnejadmojarad, T. et al. Metabolic brain disease 34.6 (2019): 1747-1759; 3. Hosseinzadeh H. Et al. Phytother Res. (2009) Jun;23(6):768-74; 4. Georgiadou, G et al. Nucroscience letters vol. 528, 1 (2012): 27-30; 5. Ahmad, Abdullah Shafique, et al. Phytomedicine. 2007 Apr;14(4):256-62. Molecules. 2020 Nov 30;25(23):5647; 8. Hosseinzadeh H, et al. Phytomedicine. 2007 Apr;14(4):256-62.







# Manufactured in-house under high quality standards



- Full control of the process and 100% traceability.
- Manufactured in Pharmactive's plant in Spain, under thorough quality standards.
- Patented extraction process developed to optimize the preservation of the actives (AFF®ON-Cool Tech).

# Manufacturing plant certifications





Quality Management System ISO 9001



Food Safety System Certified ISO 22000



Certified Environmental Management ISO 14001



#### Other certifications

Play sure doping free

TRU-ID Canada

Halal

Kosher

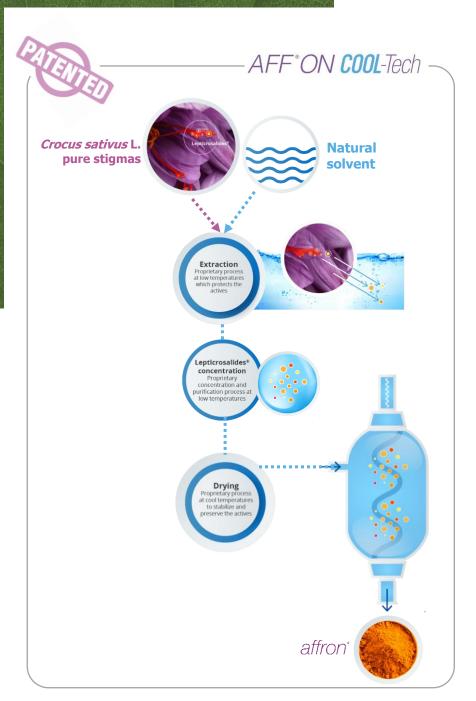












# **Exclusive green production process**

- Production process that creates highly concentrated affron® with long-lasting actives' stability of at least 36 months.
- This technique allows us to get superior saffron Quality with less industrial processing, less energy use and zero chemicals.

LESS

- Industrial processing
- Energy use

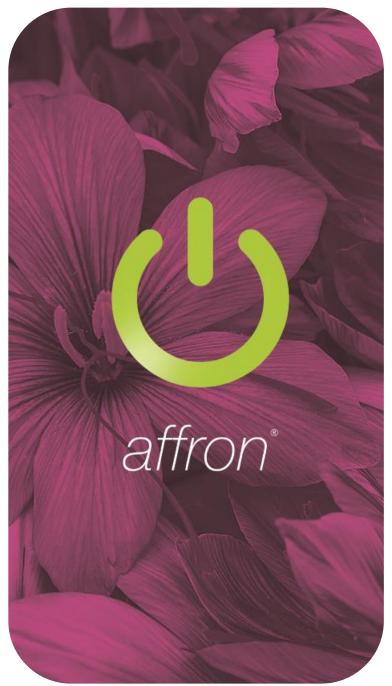
MORE

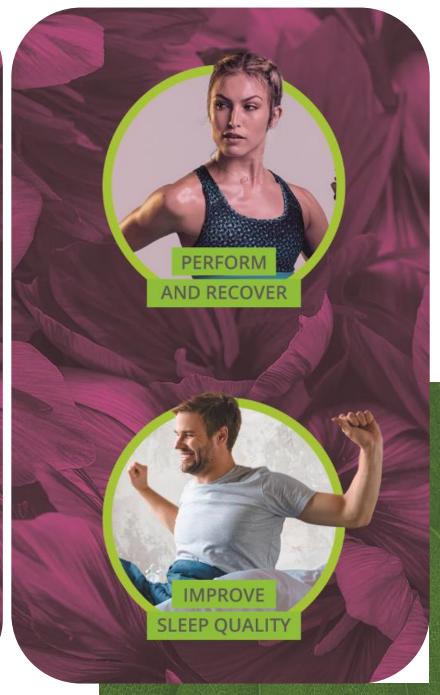
- Stability of the actives
- Actives protection
- Environment respect

**ZERO CHEMICALS** 









# THANK YOU FOR YOUR ATTENTION



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