## INSOMNIA IS A RISK FACTOR FOR:

- MORE SEVERE PSYCHIATRIC SYMPTOMS [1]
- COGNITIVE DYSFUNCTION [2]
- METABOLIC DISTURBANCES [3]
- IMPAIRED QUALITY OF LIFE [4]
- SUICIDALITY IN PATIENTS [5] WITH SCHIZOPHRENIA
- HIGH BLOOD PRESSURE [6]
- CARDIOVASCULAR DISEASE [7]
- TYPE 2 DIABETES [8]


**REFERENCES:**
**1.** Miller et al., 2021; Miller et al, 2023
**2.** Zhu et al., 2022
**3.** Freeman et al., 2019; Miller et al., 2022
**4.** Batalla-Martin et al., 2020; Xiang et al., 2009
**5.** Peng et al., 2024
**6.** Liking et al., 2021
**7.** Sofi et al., 2012; Bang et al., 2019 ; Khan et al., 2022
**8.** Anothaisintawee et al., 2015


## 4 MAIN REASONS TO CHOOSE BlueCALM®

**QUALITY**
Official and validated analytical methods

**EFFICACY**
Preclinical and clinical studies

**SAFETY**
DNA certified plant material to prevent the adulteration with hepatotoxic germander *(Teucrium species)*

**SUSTAINABILITY**
An entirely made in Italy supply chain, from the field to the final extract

DNA® CERTIFIED EXTRACTS


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# BlueCALM®

***Scutellaria lateriflora* L.** *Dry extract 10% baicalin*

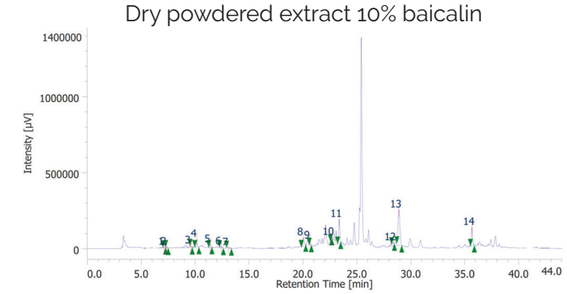
Insomnia is a widespread sleep disorder: one-third of adults suffer from it, 10%-15% report daytime symptoms associated with insomnia, and 6%-10% are diagnosed with insomnia disorder. Women are more affected, with a gender ratio of approximately 1.4 : 1. Chronic insomnia may seriously impair the quality of life and it is also a risk factor for more severe conditions.

*Scutellaria lateriflora* L. (Blue skullcap) is a perennial herb native to North America with a long traditional **use to relieve anxiety and improve mood**. Recent studies suggest neuroprotective and anxiolytic effects.

It is a rich source of constituents with known biological activity:

- **Flavonoids** (baicalin, baicalein, wogonoside, wogonin)
- **Diterpenoids** (scutelaterin A, B, and C)
- **Phenylpropanoids** (caffeic acid, cinnamic acid, coumaric acid, ferulic acid)
- **Essential oils** (terpenoids)
- **Amino acids** and **melatonin**

***Scutellaria lateriflora* L.**
Dry powdered extract 10% baicalin




HPLC-DAD chromatogram of the phenolic compounds contained in BlueCALM® (*Scutellaria lateriflora* L.) Dry extract. **1.** Gallic acid 1; **2.** Gallic acid 2; **3.** Catechin; **4.** Chlorogenic acid; **5.** Epicatechin; **6.** Caffeic acid; **7.** Siringic acid; **8.** Coumaric acid; **9.** Ferulic acid; **10.** Rutin; **11.** Benzoic acid; **12.** Cinnamic acid; **13.** Naringenin; **14.** Baicalein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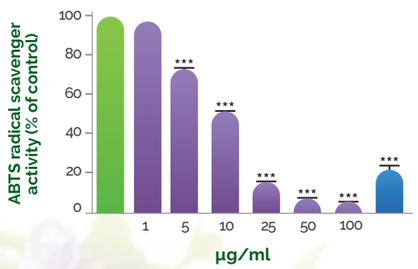
# IN VITRO STUDIES

## BlueCALM® has strong antioxidant activity showing a significant dose-dependent radical scavenger activity in different experimental models.

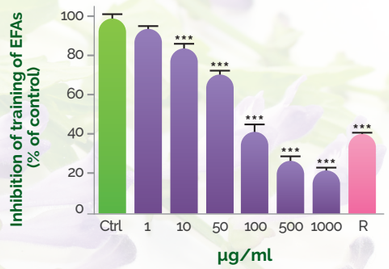



**LEGENDA**
- Ctrl
- BlueCALM®
- Trolox 10 µg/ml

Scavenger activity of BlueCALM® towards the ABTS radical.
Each value represents the mean of ± EMS (n=6).
***p<0.001 indicates a statistically significant reduction in ABTS radical levels compared to the control (Ctrl).

## BlueCALM® has shown anti-glycation activity

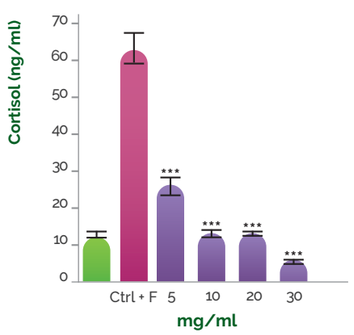
It inhibits the formation of AGEs (Advanced glycation end products), some harmful substances deriving from the combination of proteins and fats with sugars, that are involved in many chronic degenerative diseases, including Alzheimer's, and in aging. These results may support the plant's neuroprotective effects, already reported by available scientific data.




**LEGENDA**
- Ctrl
- BlueCALM®
- Rutin 50 µg/ml

Inhibition of the formation of AGEs induced by BlueCALM®. Each value represents the mean of ± EMS (n=6).
***p<0.001 indicates a statistically significant reduction in AGEs levels compared to the control (Ctrl).

## BlueCALM® significantly inhibits the cortisol release*




**LEGENDA**
- Ctrl
- Ctrl + F
- F + BlueCALM®

Concentration of cortisol (ng/mL) released from H295R cells in the basal state (Ctrl) following the treatment with forskolin (Ctrl+F), and following the treatment of cells with increasing concentrations (5-30 mg/ml) of ***S. lateriflora*** extract. Data were expressed ad mean **± SD from 3 biological replicates**.
***p<0.001

**Excess cortisol** release is associated with **many health concerns**, including psychiatric issues (i.e. anxiety, insomnia, and depression), osteoporosis, and impairment of neuroendocrine and immune systems.
**BlueCALM®** has been tested on a **human adrenocortical carcinoma cell line**, an *in vitro* model commonly used to investigate the mechanism of action of molecules with anti-anxiety activity.
**BlueCALM®** induced a **significant inhibition**, ranging from **58 to 91%**.

*Buccato, D.G.; Ullah, H.; De Lellis, L.F.; Piccinocchi, R.; Baldi, A.; Xiao, X.; Arciola, C.R.; Di Minno, A.; Daglia, M. In Vitro Assessment of Cortisol Release Inhibition, Bioaccessibility and Bioavailability of a Chemically Characterized Scutellaria lateriflora L. Hydroethanolic Extract. Molecules 2024, 29, 586. https://doi.org/10.3390/molecules29030586

# CLINICAL STUDY

## BlueCALM® was evaluated in a monocentric, randomized cross over, double blind, placebo controlled, clinical study*

**Primary endpoint:** evaluation of the effectiveness of BlueCALM in maintaining a proper sleep-wake balance (**sleep quality**).

**Secondary endpoints: sleep efficacy** (in terms of time to fall asleep, hours of sleep and efficiency of sleep), and **pain or discomfort** related to sleep.

## EVALUATION METHODS

Compilation of questionnaires:
**PSQI (sleep quality), SLEEP DIARY (sleep efficacy), VAS (pain or discomfort).**

**1 CAPSULE DAILY**
(before bedtime)
400 mg
**BlueCALM®**/capsule

**GROUP A**
33 subjects
18 - 70 years

**GROUP B**
33 subjects
18 - 70 years

**PLACEBO**

BEGINNING 1ST PERIOD — t0
t1 — 28 days
END 1ST PERIOD — t2 — 56 days

**WASH OUT PERIOD 4 WEEKS**

BEGINNING 2ND PERIOD — t3 — 84 days
t4 — 112 days
END 2ND PERIOD — t5 — 140 days

**TREATMENT**

t0 — BEGINNING 1ST PERIOD
t1 — 28 days
t2 — 56 days — END 1ST PERIOD

t3 — 84 days — BEGINNING 2ND PERIOD
t4 — 112 days
t5 — 140 days — END 2ND PERIOD

**RESULTS:** all endpoints showed a statistically significant improvement after treatment with **BlueCALM®**; none of the participants reported adverse effects from the food supplement. In all treated subjects the hours of sleep exceeded 6 hours, the minimum treshold not to develop the risk of high blood pressure, cardiovascular and metabolic disturbances, diabetes and obesity.

*Di Minno, A.; Morone, M.V.; Buccato, D.G.; De Lellis, L.F.; Ullah, H.; Piccinocchi, R.; Cordara, M.; Larsen, D.S.; Di Guglielmo, A.; Baldi, A.; et al. Efficacy and Tolerability of a Chemically Characterized Scutellaria lateriflora L. Extract-Based Food Supplement for Sleep Management: A Single-Center, Controlled, Randomized, Crossover, Double-Blind Clinical Trial. Nutrients 2025, 17, 1491. https://doi.org/10.3390/nu17091491