Calm with Zembrin®

INGREDIENTS
For centuries, *Sceletium tortuosum*, traditionally known as “kougoed” or “kanna”, has been used as a masticatory agent for the relief of thirst and hunger, as a traditional medicine, and for spiritual purposes by San and Khoikhoi people inhabiting the Cape region of South Africa. Dried plant material (aerial parts; leaves and twigs) is typically chewed and the resulting saliva and plant juices swallowed; it is also consumed in the form of teas, decoctions and tinctures. In recent years, *Sceletium tortuosum* has received a great deal of commercial interest due to its potential as an adaptogen for relieving stress in healthy people, and for improving a broad range of executive functions.* In 2009, the South African company HG&H Pharmaceuticals Pty Ltd. was granted the country's first integrated export and bioprospecting permit, allowing it to export the first standardized extract of *S. tortuosum* under the trade mark Zembrin®. Zembrin® is safe and self-affirmed GRAS (Generally Recognized As Safe) ingredient.

BENEFITS
- Doctor’s Best Calm with Zembrin® helps improve cognitive health*
- Doctor’s Best Calm with Zembrin® may help reduce feelings of stress and improve mood health*
- Doctor’s Best Calm with Zembrin® may enhance executive functions*
- Non-GMO. Soy Free. Gluten Free. Vegan

EXTENDED BENEFITS
Doctor’s Best Calm with Zembrin® helps improve cognitive health*
*Sceletium* plant species that contain alkaloids have been known to have positive and broad effects on central nervous system (CNS). Among the four major *S. tortuosum* alkaloids (mesembrine, mesembrenone, mesembrenol, and mesembranol) mesembrine and mesembrenone are the primary active constituents that have specifically shown high selectivity for the serotonin (5-HT) transporter. The standardized extract Zembrin® has also shown to inhibit both serotonin (5-HT) uptake and phosphodiesterase-4 (PDE-4). The cognitive effects of Zembrin are consistent with the in vitro structure-activity relationship analysis showing cognition is selectively mediated via the phosphodiesterase family. These biological properties highlight the potential activity of Zembrin® to improve cognitive health.*

Doctor’s Best Calm with Zembrin® may help reduce feelings of stress and improve mood health*
*Sceletium tortuosum* has a long history of human use for reducing feeling of stress and calming. Zembrin® contains the standardized extract of *S. tortuosum* that is pharmacologically safe to use in dietary supplements to promote a sense of well-being and to relieve stress.* The mechanisms of action supporting these positive effects of Zembrin® have root in the central nervous system (CNS), in particular at the level where the main constituents of Zembrin® extract interact as PDE-4 inhibitors and 5-HT reuptake blockers.*

Doctor’s Best Calm with Zembrin® may help enhance executive functions*
In general, executive functions encompass a wide variety of higher order cognitive processes that allow the flexible change of thought and behavior in response to changing cognitive or environmental situations. They are crucial for maintaining the cognitive balance of individuals in order to meet daily living tasks especially in the aging population.* The neuro-cognitive effects of extract *Sceletium tortuosum* (Zembrin®) and its main metabolites have been studied for the past decades. Zembrin® has been clinically proven to have positive effects on executive neural functions in human.*

Supplement Facts
<table>
<thead>
<tr>
<th>Serving Size</th>
<th>1 veggie capsule</th>
<th>Servings per container</th>
<th>60 servings</th>
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<tbody>
<tr>
<td>Amount per serving</td>
<td>25 mg</td>
<td>% Daily Value</td>
<td></td>
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<tr>
<td>Zembrin® (Sceletium tortuosum aerial parts extract)</td>
<td>†</td>
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† Daily Value not established.

Other Ingredients: Microcrystalline cellulose, modified cellulose (vegetarian capsule), silicon dioxide, magnesium stearate (vegetable source).

Suggested Adult Use: Take 1 capsule daily with or without food, or as recommended by a nutritionally-informed physician. Daily oral dose not to exceed 25 mg.

Warning: People taking psychiatric, anti-anxiety or anti-depressant medication should discuss the concomitant use of Zembrin-containing products with their healthcare professional.

Non-GMO / Gluten Free / Soy Free / Vegan
Color may vary.
Store in a cool dry place.

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.
A randomized, double-blind, parallel-group, placebo-controlled single center study evaluated the safety and tolerability of 2 doses (8 mg and 25 mg once daily) of Sceletium tortuosum extract, Zembrin. Participants were randomized to receive either one of 2 doses, or an identical placebo, taken once daily for 3 months. The results showed there were no apparent differences in any of the safety and tolerability parameters studied. Both doses of Zembrin®, 8 mg and 25 mg once daily, were well tolerated when used by healthy subjects.

A double-blind, placebo-controlled, cross-over study, was designed to evaluate the pharmacological effects of Zembrin® oral daily intake (25 mg) on relieving stress and improving mood health. The results showed that the dual 5-HT reuptake and PDE4 inhibitor effect of Zembrin® in the brain may be supporting the positive effect of Zembrin® on reducing stress level and improving mood health.

A randomized double-blind placebo-controlled cross-over design study evaluated the effect of 25 mg daily of Zembrin® versus placebo in 21 healthy participants. Results showed Zembrin® at 25 mg daily dosage significantly improved cognitive set flexibility and executive function, compared to the placebo group. Positive changes in mood and sleep were also found in the Zembrin® group. Zembrin® was well tolerated as well. The study presented a promising cognitive enhancing effects of Zembrin®.

A toxicological safety assessment of Zembrin® was conducted in rats at different dosages during 14-day and 90-day studies. No signs of toxicity that were considered related to administration of Zembrin® by gavage were observed in male or female Wistar rats at doses 100, 300, 450, and 600 mg/kg bw/day for 90 consecutive days. The NOAEL (No Observed Adverse Effect Level) was determined to be 600 mg/kg body weight/day (bw/day). Applying a 100-fold uncertainty factor to compensate for inter- and intra-species differences, results can be extrapolated to an acceptable daily intake of 420 mg by a 70 kg human. Zembrin® is intended to be used as an ingredient in dietary supplements. The recommended consumption is 25 mg per day. This is 0.357 mg/kg bw/day in a 70 kg adult, which is 1680 times less than the NOAEL of 600 mg/kg bw/day.