World leading producer of quality wild harvested *Rhodiola rosea*
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Nektium is the global market leader in the production of outstanding quality Rhodiola rosea extracts.

One of our founders, Dr. Zakir Ramazanov first observed the endurance enhancing effects of this powerful adaptogen when he was serving in the Russian army in Afghanistan and soon after pioneered its worldwide use.

SUPERIOR RAW MATERIAL
Nektium is one of a few select companies in the world that are authorized by a special permit issued by the Russian Government to export Rhodiola rosea from the pristine Altai Mountains in Siberia with a loyal supplier relationship that spans more than 20 years.

GUARANTEED BIOACTIVES
We pride ourselves on being true specialists in the production of outstanding Rhodiola rosea and vouch for the specified levels of Rhodiolife®’s key bioactives.

COMPETITIVE PRICING AND FLEXIBILITY
As we control the whole supply chain of our Rhodiola rosea roots, we are able to offer you competitive prices. We provide Rhodiolife® in two bioactive grades and can also standardize it to your customized specifications.

Rhodiolife®)

What is Rhodiolife®?
Rhodiolife® is Nektium’s standardized extract of Rhodiola rosea roots, available in two specifications: ≥ 3% total rosavins and ≥ 1% salidroside and ≥ 5% total rosavins and ≥ 1.8% salidroside.

How does Rhodiolife® work?
Rhodiolife® is a powerful adaptogen that produces a non-specific state of adaptation and resistance in the body to physical, emotional and environmental stress. Rhodiolife® is experiential, a distinct advantage over other adaptogens. Even a single dose provides tangible activation of mental energy and improved focus.
I. INTRODUCTION

ACTIVE PRINCIPLES OF RHODIOLIFE®

The adaptogenic activity of *Rhodiola rosea* is usually attributed to the presence of four principal active ingredients: salidroside, rosin, rosinavin and rosarin.

**Bioactive compounds**

![Salidroside](salidroside.png)

- Salidroside

![Rosarin](rosarin.png)

- Rosarin

![Rosavin](rosavin.png)

- Rosavin

![Rosin](rosin.png)

- Rosin

UHPLC chromatogram of *Rhodiola rosea* roots above, compared with our Rhodiolife® extract.

Chemical structures of the main quantified bioactive compounds in *Rhodiola rosea* roots.
II. SCIENTIFIC AND CLINICAL RESEARCH

An extensive scientific literature has validated many of the traditional Siberian uses of *Rhodiola rosea* roots for adaptogenic, mental energy and endurance-enhancing effects.

Nektium and partners have built on this impressive research base with preclinical and clinical studies on Rhodiolife® that have demonstrated rapid onset of brain-activating activity, increased Long-Term Potentiation, anxiolytic and antidepressant potential, anti-inflammatory and neuroprotective activity, enhanced physical work capacity and recovery, and skeletal muscle protective activity.

Rhodiolife® is a highly versatile, experiential adaptogen that can be used in mental energy, mood, nootropic and sports performance products.
# II. SCIENTIFIC AND CLINICAL RESEARCH

## 1. MENTAL ENERGY

While many studies on various extracts and formulations of *Rhodiola rosea* have demonstrated benefits in diverse models of physical and psychological stress, Nektium pioneered the investigation of the Central Nervous System (CNS) activities of Rhodiolife® using cutting-edge neurophysiological studies including *in vivo* functional electroencephalogram (EEG). In a preclinical study, a single dose of Rhodiolife® was demonstrated to result in a very rapid onset of brain activation on EEG, an effect that had a long duration of action, lasting at least five hours.

The EEG signature was shown to be very similar to the signatures for caffeine, Guarana (*Paullinia cupana*) and *Ginkgo biloba*.

A second approach for the pharmacological characterization of botanical preparations involves elucidating the direct action on brain matter. For this purpose, we used an *in vitro* hippocampal slice preparation from adult rats.

*In vitro* Long-Term Potentiation (LTP) studies in the hippocampus were performed and changes of population spike amplitude as a consequence of Single stimuli challenge (SS) and Theta burst stimulation (TBS) were recorded.

Rhodiolife® increases LTP\(^1\), an effect related to improvements in spatial and temporal memory that enables the brain to form memories and helps athletes to automate coordination skills\(^4\).

### Table: Increased Long-Term Potentiation

<table>
<thead>
<tr>
<th>Amplitude [mV]</th>
<th>Rhodiola TBS</th>
<th>Rhodiola SS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>×3</td>
<td>×4</td>
</tr>
<tr>
<td>0.5</td>
<td>×2</td>
<td>×3</td>
</tr>
<tr>
<td>1</td>
<td>×1</td>
<td>×2</td>
</tr>
<tr>
<td>1.5</td>
<td>×0.5</td>
<td>×1</td>
</tr>
<tr>
<td>2</td>
<td>×0.5</td>
<td>×0.5</td>
</tr>
<tr>
<td>2.5</td>
<td>×0.5</td>
<td>×0.5</td>
</tr>
<tr>
<td>3</td>
<td>×0.5</td>
<td>×0.5</td>
</tr>
<tr>
<td>3.5</td>
<td>×0.5</td>
<td>×0.5</td>
</tr>
<tr>
<td>4</td>
<td>×0.5</td>
<td>×0.5</td>
</tr>
<tr>
<td>4.5</td>
<td>×0.5</td>
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### Diagram: EEG Rhodiolife®

- **Front. cortex**
  - Spectral power [% of pre-drug baseline]
  - 5-65 min: 100
  - 65-125 min: 100
  - 125-185 min: 100
  - 185-245 min: 100
  - 245-305 min: 100

- **Hippocampus**
  - Spectral power [% of pre-drug baseline]
  - 5-65 min: 100
  - 65-125 min: 100
  - 125-185 min: 100
  - 185-245 min: 100
  - 245-305 min: 100

**Note:** Rhodiolife SS

**Figure:**

- **EEG Rhodiolife®**
  - Spectral power [% of pre-drug baseline]
  - 5-65 min: 100
  - 65-125 min: 100
  - 125-185 min: 100
  - 185-245 min: 100
  - 245-305 min: 100

**Legend:**

- *p<0.10
- **p<0.05
- ***p<0.01

**Graph:**

- **Increased Long-Term Potentiation**
  - Amplitude [mV] vs. Concentration [mg/L]
  - Rhodiola TBS: ×3
  - Rhodiola SS: ×4

**Graph Notes:**

- **α1 β1bβ1a β2 ϒ δ ϑ α1 α2 β1bβ1a β2 ϒ**

**Graph Scale:**

- **0 2.5 10 20 mg/L**
II. SCIENTIFIC AND CLINICAL RESEARCH

2. MOOD
In a pilot study of Rhodax®, a marketed finished product containing Nektium’s Rhodiolife®, 10 participants diagnosed with Generalized Anxiety Disorder (GAD) received a daily dose of 340mg for 10 weeks, had significantly reduced Hamilton Anxiety Rating Scale (HARS) scores.6

Rhodiola rosea rhizome was studied in two randomized, double-blind, placebo-controlled trials of 146 subjects with major depressive disorder and seven open-label studies totaling 714 individuals with stress-induced mild depression. The results of these studies suggest a possible antidepressant action for Rhodiola rosea extract.6

3. NEUROPROTECTION
Reports have indicated neuroprotective potential for Rhodiola rosea.7 The effect of Rhodiolife® on genes related to neurodegeneration and neuroprotection was tested in the cholinergic neuroblastoma cell line NS20Y. The gene modulation profile showed a significant upregulation (p<0.05) of 3 GPCR-genes, suggesting a possible role for Rhodiolife® in neuroprotection.8

4. ANTI-INFLAMMATORY ACTIVITY
In a study performed in rats, an ethanolic Rhodiola rosea extract inhibited formaldehyde-induced arthritis and nystatin-induced paw oedema in a dose-dependent manner. The results demonstrated that Rhodiola rosea decreases inflammation and reduces COX-2.9

5. SPORT & MUSCLE HEALTH
Rhodiolife® protects muscle cells against oxidative stress10, improves physical work capacity, assists recovery11 and protects the muscle tissue of healthy untrained volunteers during exercise12. Rhodax® (Rhodiolife®) was studied in a randomized controlled clinical trial, where 36 healthy untrained volunteers were divided into 3 groups (control, placebo and Rhodiolife®).

Individuals received placebo or 340mg of Rhodiolife® for 30 days before and 6 days after exhausting physical exercise on a cycle ergometer. In the group treated with Rhodiolife®, CRP (C-reactive protein) increases were smaller than in the control and placebo groups and had returned to normal levels five days after exercise.

As expected, the mean CK (creatine kinase) level in the blood increased significantly after exhausting physical exercise in all groups, and 5 days after exercise, the CK activity in the Rhodiolife*-treated group was significantly lower than in the placebo and control groups. Thus, treatment of untrained volunteers with Rhodiolife® reduced inflammation, evidenced by decreased CRP, CK and reduced muscle damage.
6. IMPROVED ENDURANCE EXERCISE PERFORMANCE

The effect of acute Rhodiola rosea intake on physical capacity, muscle strength and speed of limb movement was tested in a double-blind, randomized placebo-controlled study (200mg, 3% rosavin + 1% salidroside, n= 24).

Rhodiola rosea intake increased time to exhaustion (p<0.05) and VO_{2}max (p<0.05), indicating that Rhodiola rosea can improve endurance exercise capacity in healthy young volunteers.

A second study analyzed the effect of Rhodiola rosea on endurance exercise performance and perceived exertion in a double-blind, random crossover manner (3mg/kg, n= 18) in a bicycle ergometer trial. Perceived exertion (RPE) was measured every 5 minutes. Subjects completed the trial significantly faster after Rhodiola rosea ingestion and the mean RPE was lower. Acute Rhodiola rosea ingestion appeared to improve endurance exercise performance by decreasing the perception of effort.

7. IMPROVED PHYSICAL WORKING CAPACITY AND RECOVERY

Comparison of Rhodiola rosea and Rhodiola crenulata showed that Rhodiola rosea is more effective than Rhodiola crenulata at improving physical work capacity. The effect of Rhodiola rosea supplementation on ATP (adenosine triphosphate) content in muscles was studied in rats that ingested Rhodiola rosea (50mg/kg bw) and Rhodiola crenulata (50mg/kg bw) in a forced swim test.

The results suggest that rosavins, only present in Rhodiola rosea, may be responsible for the improved physical work capacity and recovery.

8. HEAT SHOCK PROTEIN (HSP70) IMPROVES MUSCLE PROTECTION AND RECOVERY

The expression of heat shock proteins (HSP) is one of the essential stress reactions of cells. Acute endurance and resistance protocols increase the muscle content of several HSP, contributing to muscle regeneration and recovery.

While additional work is needed to confirm the findings, recent data suggest that Rhodiolife® modifies the production of HSP70 in muscle cells under conditions of increased oxidative stress, such as that caused by intense physical exercise and protects muscles from stress related damage.

Cell cultures without Rhodiolife® pre-treatment showed a 25% decrease in cell viability following exposure to H_{2}O_{2}, while no significant decrease in cell viability was detected in cells pre-treated with Rhodiolife®. Rhodiolife® increases expression of HSP70 genes.

HSP70 protein levels were maintained in cell cultures pre-treated with Rhodiolife® but were significantly lower (~50%) in cells exposed to H_{2}O_{2} without Rhodiolife® treatment (p= 0.05 compared to control).

![Protection of HSP70](image-url)
9. POSSIBLE IMMUNE SUPPORT IN SPORTS

Ground-breaking studies led by Dr. David Nieman, director of the Appalachian State University Human Performance Laboratory at the NC Research Campus (NCRC) in Kannapolis, demonstrated that in the presence of serum from Rhodiolife® and placebo supplemented subjects, Rhodiolife® protects against virus replication (p= 0.03).

These findings suggest that bioactive compounds in the serum of subjects ingesting Rhodiolife® may be protective against virus replication following intense and prolonged exercise, a finding that needs verification in future studies\(^\text{16}\).

QUALITY ASSURANCE & CERTIFICATIONS

Rhodiolife® is the result of high quality botanical raw material and meticulous manufacturing procedures. Nektium’s facilities and production processes strictly comply with cGMP (independently audited and certified annually) and rigorous quality control programs that ensure a high quality product.

Nektium Pharma S.L. is authorized by the Spanish Health & Food Agency for the production of botanical and fruit extracts in conformance with RD 1712/1991 and Spanish Regulations.

III. MANUFACTURING PROCESS

DNA BARCODING: IDENTIFICATION OF SPECIES

Botanical raw material first undergoes macroscopic inspection to ensure it conforms with reference plant material. DNA barcoding by the Royal Botanical Garden, Madrid, is used to positively confirm its botanical identity.

Additionally, UHPLC chromatographic profiles are used to confirm the presence of characteristic markers and to quantify the content.


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