Redefines the Standard in Sports Nutrition

3 in 1 Performance - ENDURANCE, ENERGY, RECOVERY

Validated in 1 in-vivo and 5 human clinical trials

Published in PLOS One
Journal of Ginseng Research
Journal of the International Society of Sports Nutrition
Evidence-based Complimentary and Alternative Medicine
Journal of Functional Foods

Patent App. 15/989, 704

GRAS/NDI self-affirmed
NPN 80086984

Pennies per serving

nulivscience.com | actigin.com
ActiGin® is NuLiv Science’s proprietary sports nutraceutical composed of two highly purified and fractionated extracts from *Panax notoginseng* and *Rosa roxburghii* produced by a NuLiv Science pharmaceutical extraction and processing technology.

ActiGin® is the result of over ten years of research that has shown in one *in-vivo* and five human clinical trials published in *PLOS One*, *Journal of Ginseng Research* and *Journal of the International Society of Sports Nutrition* to:

- increase endurance time (time to exhaustion) by 20% in a high-intensity (80% V0₂max) cycling exercise time to exhaustion in human clinical trial. Published in *PLOS One*.

- increase energy production by producing 47% more pace-making enzyme Citrate synthase in the citric acid cycle (ATP production) in muscle cells in a vigorous (70% V0₂max) 60 minute cycling exercise in another human clinical trial published in *PLOS One*.

- speed up muscle recovery by reducing inflammation in muscles (24% in TBARS, 44% in MDA, 35% in IL-6, and 69% in CK) and increasing muscle glycogen buildup by 273% in a vigorous (70% V0₂max) 60 minute cycling exercise or a weight lifting exercise in a third human clinical trial published in *PLOS One*.

- eliminate senscent muscle cells through macrophage phagocytosis in a fourth human clinical trial published in *Journal of Ginseng Research*. Specifically, to decrease SA-β-gal and collagenase, reverse apoptotic DNA fragmentation and leukocyte infiltration, and increase iNOS and IL-6 mRNA expression in quadriceps (*vastus lateralis*) after a 60 minute cycling exercise at 70% V0₂max.

- effectively facilitate senescent cell clearance in contracting muscles and helps maintain muscle stem cell numbers during exercise to enhance high intensity endurance performance.

For details, please see “View Scientific Papers”
HOW ACTIGIN® WORKS

One *in-vivo* and three human clinical trials on ActiGin® suggest that its effects on improving endurance/stamina, energy and recovery time in high-intensity exercises may be due to its ability to preserve insulin receptors and glucose transporters on muscle membrane during intensive exercises to ensure a continuous supply of blood glucose into muscle. Glucose is the fuel for muscle during intensive exercise. Depletion of glucose has detrimental effects for muscles to contract and work properly.

There are senescent cells in all human tissues at certain proportions, particularly for those short-lived endothelial cells (lifespan < 2 weeks) in blood vessels of tissues. ActiGin® substantially reduced senescent cell population (mostly endothelial progenitor cells) of exercising skeletal muscle (JGR). Exercise challenge acutely decreases satellite cell numbers due to increased demand on nucleus for muscle regeneration during challenges. ActiGin® completely attenuated acute satellite cell depletion (JFF). These findings suggest that ActiGin® effectively facilitates senescent cell clearance in contracting muscles and helps maintain muscle stem cell numbers during exercise to enhance high intensity endurance performance.

*For details, please see "View Scientific Papers"
**Endurance**

**ActiGin® Improves 60 Min High-Intensity Cycling (80% VO₂ Max) Time to Exhaustion by 20% (1,2)**

ActiGin® was shown in a randomized double-blind placebo controlled crossover human clinical trial (1) to increase the time to exhaustion in high-intensity cycling (80% VO₂ max) by 20%.

Based on the findings from the other human clinical trials on ActiGin®, we propose that the improved endurance may be due to ActiGin®’s ability to meet the increased energy demand in glycogen and ATP in muscle during intense exercise by increasing ATP (in citrate synthase (1)) production, by preserving the insulin pathway to mitigate the interruption of glucose supply to muscle cells (1), and by scavenging the senescent muscle cells produced during the intense exercise (2).

### Study Design on ActiGin®’s Ergogenic Action

ACTIGIN® INCREASES ENERGY LEVEL IN 60 MIN CYCLING (70% VO₂ MAX) BY 47% (1)

ActiGin® was shown in a randomized double-blind placebo controlled crossover human clinical trial (1) to increase the citrate synthase in muscle by 47% after a 60 min cycling exercise at 70% VO₂ max. Citrate stands as a pace-making enzyme in the first step of the citric acid cycle that produces ATP, the energy currency of cells.

Relative citrate synthase activity in indicated time after exercise

<table>
<thead>
<tr>
<th>Time After Exercise</th>
<th>Placebo Group</th>
<th>ActiGin® Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 hrs</td>
<td>100.0±12.38</td>
<td>94.60±12.43</td>
</tr>
<tr>
<td>3 hrs</td>
<td>100.0±14.76</td>
<td>147.23±19.77*</td>
</tr>
</tbody>
</table>

*Significant difference against placebo group., p<0.05

Study Design on ActiGin®'s Anti-inflammatory Effect on Muscles After Exercise

**ACTIGIN® SPEEDS UP MUSCLE RECOVERY BY MITIGATING INFLAMMATORY RESPONSE AFTER STRENUOUS EXERCISE (1, 2)**

- Reduces lipid peroxidation marker TBARS by 24% after a 60 min cycling exercise at 80% VO₂ max (1).
- Reduces free radical damage to muscle after exercise (MDA synthesis) by 44% on day 4 after a weight lifting exercise.
- Reduces inflammation by decreasing IL-6 synthesis by 35% on day 4 after a weight lifting exercise.
- Decreases CK (Creatine Kinase) on day 4 by 69% after a weight lifting exercise.

Plasma CK reflects leakage of protein from skeletal muscle to circulation, which normally occurs after vigorous exercise.

Prolonged exercise increases cellular membrane peroxidation (mirrored by increased TBARS or MDA), which has been suggested to disrupt normal cellular insulin and glucose signaling pathways on sarcolemma and glycogen synthesis in muscles. ActiGin® minimizes such unwanted oxidative damage produced during physical exertion, and ultimately enhances the robustness of our body to sustain prolonged intensive exercise.


ACTIGIN® SPEEDS UP MUSCLE RECOVERY BY INCREASING MUSCLE GLYCOGEN SYNTHESIS (1)

Subjects performed an acute bout of 60 min of cycling at 70% VO₂ max. Vastus lateralis samples were collected at 0 h and 3 h post-exercise for determining the rate of glycogen storage. The rate of 3 h glycogen accumulation was elevated by 2.73 fold with ActiGin® ingested the night before and immediately after a glycogen-depleting exercise.

Muscle glycogen is the main fuel for strenuous sports activity. ActiGin® increased the rate of glycogen re-synthesis after 1 h cycling at 70% VO₂ max by 373%. This 2.73 fold increase improves fatigue recovery from acute physical challenge for prolonged aerobic and anaerobic activities. It is suggested that the mechanism may be due to its ability to up-regulate the Adiponectin secretion to affect AMPK-GLUT4 mediated glucose absorption in muscle cells.

1. C.H. Kuo, John L. Ivy, etc. Improved Inflammatory Balance of Human Skeletal Muscle during Exercise after Supplementation of the Ginseng-Based Steroid ActiGin®. PLOS One, 2015, DOI:10.1371/journal.pone.0116387
**ACTIGIN® REDUCES INFLAMMATION IN EXHAUSTED EXERCISE-INDUCED SARCOLEmma LIPID PEROXIDATION IN RATS (3)**

Exercise-induced oxidative stress causes temporally membrane lipid peroxidation (MDA level), which was protected by ActiGin® supplementation by preserving the GSH/GSSG ratio. Sarcolemma integrity is essential for transmembrane glucose transport and normal insulin signaling. Normal insulin signaling is required for triggering muscle glycogen synthesis.

ACTIGIN® ELIMINATES SENESCENT MUSCLE CELLS (2)

- Decreases SA-β-gal, a biomarker of senescent cell*
- Reverses apoptotic DNA fragmentation, a key feature of apoptosis*
- Reverses leukocyte infiltration in muscle faster*
- Increase in iNOS mRNA expression in muscle suggests an enhanced phagocytic function of macrophage*
- Increase in IL-6 mRNA expression in muscle suggests an enhanced phagocytic function of macrophage*
- Decrease in collagenase attenuated inflammatory collagenase activation*

*In vastus lateralis after a 60 min cycling at 70% VO₂ max

A Representative immunohistochemical staining images showing SA-β-gal (brown stain indicated by arrows) in vastus lateralis muscle of a participant.

(B) ActiGin® supplementation 1 h before exercise decreases SA-β-gal in vastus lateralis muscle after a 1 h cycling at 70% VO₂ max.
(A) Representative images for apoptotic DNA fragmentation (green, indicated by arrows) and DAPI (4,6-diamidino-2-phenylindole) nuclei (blue) in vastus lateralis muscle cross-section.

(B) Exercise increases the number of apoptotic nuclei for both PLA and ActiGin® trials.

(C) ActiGin® supplementation 1 h before exercise reverses apoptotic nuclei in vastus lateralis muscle during a 3 h recovery.
LEUKOCYTE INFILTRATION IN HUMAN MUSCLE AFTER EXERCISE

(A) Representative hematoxylin and eosin staining images showing leukocyte infiltration (arrow) in vastus lateralis muscle cross-section of a participant.

(B) Leukocyte infiltration increases after exercise in both PLA and ActiGin® trials.

(C) Leukocyte infiltration reverses faster during a 3-h recovery in the ActiGin® trial compared against the PLA trial.
CD68+ MACROPHAGE INFILTRATION IN HUMAN MUSCLE AFTER EXERCISE

(A) Representative immunofluorescence staining images showing CD68+ cells (green) in vastus lateralis muscle cross-section.

(B) CD68+ macrophage increases after 1 h cycling at 70% VO₂ max during both PLA and ActiGin® trials.
(A) iNOS mRNA level in vastus lateralis shows an earlier increase during the ActiGin® trial.

(B) IL-6 mRNA level increases after exercise in both PLA and ActiGin® trials. During a 3 h recovery, this increase is further amplified, to a greater extent, for the ActiGin® trial above the PLA trial.

(C) Collagenase activity increases after exercise only in the PLA trial. Collagenase activity is lower in the ActiGin® trial, compared with the PLA trial after a 3 h post-exercise recovery.
**ACTIGIN® IMPROVES ENDURANCE/STAMINA AND RECOVERY BY ACCELERATING THE REPAIR AND REGENERATION OF EXERCISING SKELETAL MUSCLES**

Endurance or high-intensity exercise increases muscle damage. Yet, muscle damage indices muscle repair, regeneration and growth. The key is to activate Myf5 gene expression that leads to satellite cell activation, proliferation, differentiation and nucleus fusion. Satellite cell availability determines the resilience of muscle against physical challenges.

ActiGin® was shown in a double-blind, placebo-controlled crossover human study published in the Journal of Functional Foods to increase the Myf5 mRNA by 81% that leads to satellite cell activation, proliferation, differentiation and nucleus fusion into existing muscle tissue. The accelerated myogenesis of exercising skeletal muscles may explain the improved high intensity endurance performance.

5. C. H. Kuo, etc. Satellite cell depletion in exercising human skeletal muscle is restored by ginseng component Rg1 supplementation. *Journal of Functional Foods.*
ACTIGIN® INCREASES MYF5 mRNA EXPRESSION OF HUMAN SKELETAL MUSCLE IMMEDIATELY AFTER 60 MIN CYCLING (70% VO₂ MAX) BY 81% (5)

ActiGin® was shown in a randomized double-blind placebo-controlled crossover human clinical trial (5) to increase the Myf5 mRNA expression by 81% immediately after a 60 min cycling exercise at 70% VO₂ max. Induction of Myf5 mRNA expression is generally regarded as a hallmark for commitment of myogenesis.

Myf5 mRNA in exercising human skeletal muscle. Expression levels are normalized to baseline (Pre). Values are expressed as means±SE (N=12). *Significantly different from baseline (Pre), P<0.05. †Significantly different from PLA, P>0.05. PLA:Placebo.

5. C. H. Kuo, etc. Satellite cell depletion in exercising human skeletal muscle is restored by ginseng component Rg1 supplementation. Journal of Functional Foods.
ActiGin® received US GRAS/NDI self affirmation in April, 2015 from AIBMR, Washington, USA. The affirmation was based on the 28-dayRepeated Oral Dose Toxicity Study in Rats completed in December, 2014 by TOXI-COOP ZRT. The NOAEL (No Observed Adverse Effect Level) is 600 mg/kg bw/day, and many toxicity studies on Panax notoginseng and Rosa roxburghii in published papers.

View Scientific Papers

C. H. Kuo, John L. Ivy, etc. Improved inflammatory balance of human skeletal muscle during exercise after supplementations of the sinseng-based steroid Rg1. PLOS One, 2015, DOI:10.1371/journal.pone.0116387.
C. H. Kuo, etc. Ginsenoside-Rg1 protects the liver against exhaustive exercise-induced oxidative stress in rats. Evidence-based Complementary and Alternative Medicine. 2012 (932185):8.
C. H. Kuo, etc. Satellite cells depletion in exercising human skeletal muscle is restored by ginseng component Rg1 supplementation. Journal of Functional Foods.
For questions and additional information please contact

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