RESEARCH OVERVIEW

SENACTIV

Unleashing ACTIV Performance



nulivscience.com

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We are committed to the dissemination of accurate and unbiased information. Our goal is to contribute to the understanding of its potential benefits and limitations. For any inquiries, clarifications, or further information, please do not hesitate to contact us.

Thank you for your interest in our research overview.



MUSCLE ENERGY & REGENERATION

Validated in 3 in-vivo and 5 human clinical trials

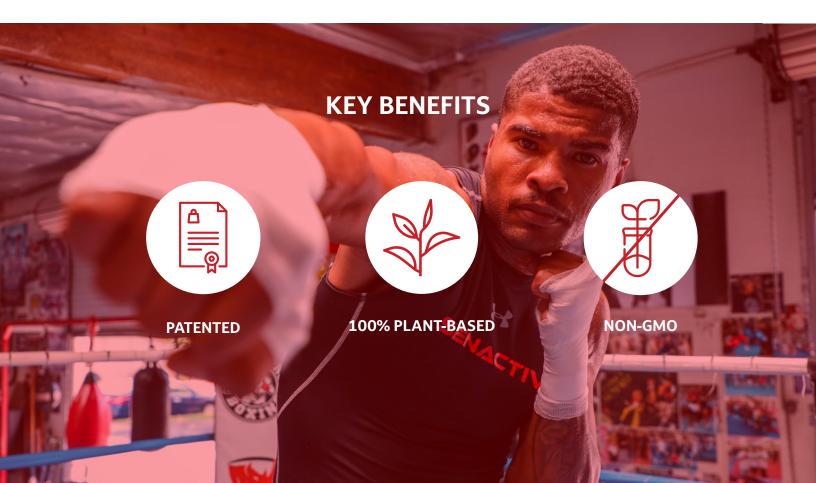
Published in PLOS One Journal of Ginseng Research Journal of the International Society of Sports Nutrition Evidence-based Complimentary and Alternative Medicine Journal of Functional Foods Journal of Science in Sport and Exercise Aging

US Patent No. 10,806,764

NPN 80086984

GRAS/NDI Self-affirmed

Pennies per serving



DISCOVER SENACTIV®

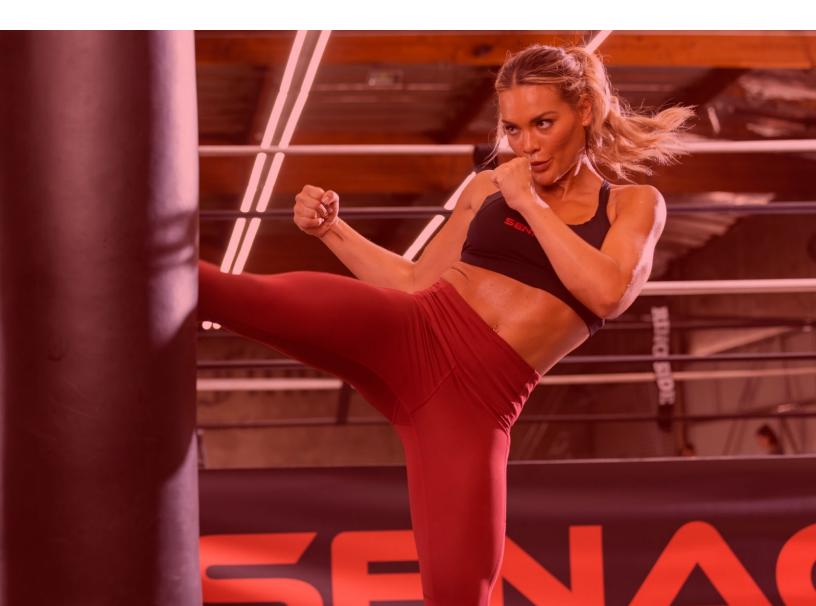
Senactiv[®] is a NuLiv Science sportceutical composed of highly purified and fractionated extracts from *Panax notoginseng* and *Rosa roxburghii*.

Senactiv[®] is the result of over ten years of research, supported by 9 published papers across various scientific journals, including PLOS One, Journal of Ginseng Research, Journal of the International Society of Sports Nutrition, Evidence-based Complimentary and Alternative Medicine, Journal of Functional Foods, Journal of Science in Sport and Exercise, and Aging. The research findings indicate that Senactiv[®]:

- Supports Enhanced Endurance: In a human clinical trial published in PLOS One, Senactiv[®] increased endurance (time to exhaustion) by 20% during high-intensity cycling exercise at 80% VO2max.
- Boosts Energy Production: Senactiv[®] promoted energy production by stimulating a 47% increase in citrate synthase, a key enzyme in the citric acid cycle responsible for ATP production, during a vigorous 60-minute cycling exercise at 70% V02max, as reported in a human clinical trial published in PLOS One.
- Accelerates Muscle Recovery: During both vigorous cycling and weight lifting exercises, Senactiv[®] demonstrated reduced muscle inflammation (24% in TBARS, 44% in MDA, 35% in IL-6) and increased muscle glycogen buildup by 273%. These findings were published in PLOS One.
- Fosters Healthy Muscle Cells: In a study featured in the Journal of Ginseng Research, Senactiv[®] demonstrated the ability to clear senescent muscle cells through macrophage phagocytosis, resulting in decreased SA-βgal and collagenase, reversal of apoptotic DNA fragmentation, reduced leukocyte infiltration, and increased iNOS and IL-6 mRNA expression in quadriceps (vastus lateralis) after a 60-minute cycling exercise at 70% V02max.
- Supports Muscle Regeneration: Senactiv[®] promotes the restoration of satellite cell numbers and total glutathione levels, along with centrally nucleated myofibers, 3 hours post-exercise, as observed in a study published in the Journal of Functional Foods. Satellite cells play a crucial role in muscle cell differentiation.

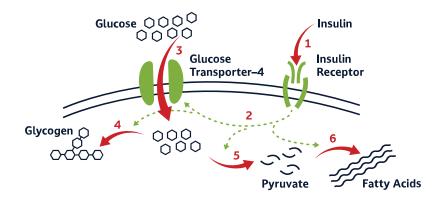
- Clears Senescent Cells: Senactiv[®] demonstrated the ability to effectively clear senescent cells in active muscle and stimulate tissue repair after a 60-minute VO2max cycling exercise by the clearance of P16^{INK4α} and decreased IL-10 mRNA, as shown in a human clinical trial published in Aging.
- Promotes Overall Cell Renewal and Growth: Senactiv[®] decreases senescent cells and triggers cell renewal and growth, contributing to potential increase in physical fitness and muscle longevity.

In summary, Senactiv[®] has demonstrated benefits in enhancing endurance, boosting energy production, accelerating muscle recovery, fostering muscle cell health, supporting muscle regeneration, clearing senescent cells, and promoting overall cell renewal and growth in various clinical studies published in reputable scientific journals.



HOW SENACTIV® WORKS

MECHANISM OF ACTION



Endurance & Energy
Centrally nucleated myofiber 🛧
Nucleated Myofibers 个
Glycogen Replenishment 🛧
Citrate Sunthase 个
Insulin Sensitivity 🛧
Glutathione 个
IL-6 1
Myf5 🔨
Pax7 1

Muscle Fatigue Recovery

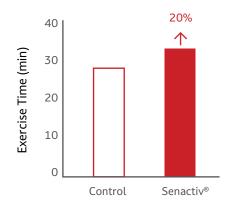
Apotatic nuclei \checkmark SA- β -gal \checkmark P16^{inka+} \checkmark TBars \checkmark MDA \checkmark TNF-a \checkmark IL-10 \checkmark IL-6 \checkmark CK \checkmark

Among the studies conducted on Senactiv[®], including an in-vivo trial and three human clinical trials, there is evidence to suggest that its effects on enhancing endurance, energy, and recovery during high-intensity exercise may be attributed to its potential role in preserving insulin receptors and glucose transporters on muscle cell membranes, ensuring a consistent supply of blood glucose to fuel active muscles. Senactiv[®] has also shown promise in reducing the population of senescent cells, particularly endothelial progenitor cells, in active skeletal muscle, as reported in the Journal of Ginseng Research (JGR). Additionally, it counteracts the temporary depletion of satellite cells responsible for muscle regeneration during exercise, as noted in the Journal of Functional Foods (JFF). These findings collectively suggest that Senactiv[®] may effectively facilitate senescent cell clearance and help maintain muscle stem cell numbers during exercise, potentially enhancing high-intensity endurance performance.

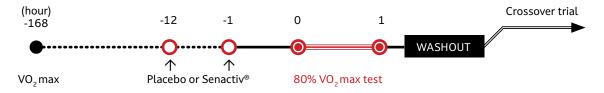
ENDURANCE SENACTIV[®] IMPROVES 60 MIN HIGH-INTENSITY CYCLING (80% VO₂MAX) TIME TO EXHAUSTION BY 20%^{1,2}

In a randomized double-blind placebo-controlled crossover human clinical trial, Senactiv[®] demonstrated a notable 20% increase in the time to exhaustion during high-intensity cycling at 80% VO2 max.

Building upon the insights gained from various other human clinical trials involving Senactiv[®], it is plausible to suggest that the observed enhancement in endurance could be attributed to several factors. Senactiv[®] appears to meet the heightened energy demand in muscles during intense exercise by boosting ATP production through an increase in citrate synthase. Additionally, it may contribute to sustained exercise performance by allowing an uninterrupted supply of glucose to muscle cells. Furthermore, Senactiv[®] seems to play a role in reducing the presence of senescent muscle cells generated during intense exercise, which could collectively contribute to improved endurance.



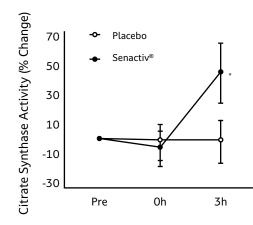




- Hou, C.-W., Lee, S.-D., Kao, C.-L., Cheng, I.-S., Lin, Y.-N., Chuang, S.-J., ... Kuo, C.-H. (2015). Improved Inflammatory Balance of Human Skeletal Muscle during Exercise after Supplementations of the Ginseng-Based Steroid Rg1. *Plos One*, 10(1). doi: 10.1371/journal.pone.0116387
- Wu, J., Saovieng, S., Cheng, I.-S., Liu, T., Hong, S., Lin, C.-Y., ... Kuo, C.-H. (2018). Ginsenoside Rg1 supplementation clears senescence-associated β-galactosidase in exercising human skeletal muscle. *Journal of Ginseng Research*. doi: 10.1016/j.jgr.2018.06.002

ENERGY SENACTIV[®] INCREASES ENERGY LEVEL IN 60 MIN CYCLING (70% VO₂MAX) BY 47%¹

Senactiv[®] demonstrated in a randomized double-blind placebo-controlled crossover human clinical trial to increase the citrate synthase in muscle by 47% after a 60 min cycling exercise at 70% VO2 max. Citrate synthase stands as a pace-making enzyme in the first step of the citric acid cycle, responsible for ATP production—the energy currency of cells.

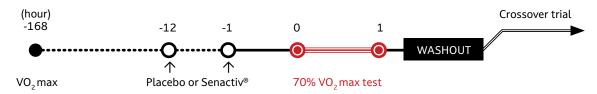


Relative citrate synthase activity in indicated time after exercise

CS Activity (%)	Placebo Group	Senactiv [®] Group
0 hrs After Exercise	100.0±12.38	94.60±12.43
3 hrs After Exercise	100.0±14.76	147.23±19.77*

*Significant difference against placebo group., p<0.05

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



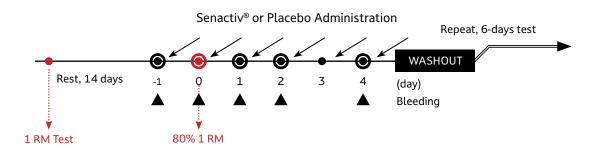
 Hou, C.-W., Lee, S.-D., Kao, C.-L., Cheng, I.-S., Lin, Y.-N., Chuang, S.-J., ... Kuo, C.-H. (2015). Improved Inflammatory Balance of Human Skeletal Muscle during Exercise after Supplementations of the Ginseng-Based Steroid Rg1. *Plos One*, 10(1). doi: 10.1371/journal.pone.0116387

RECOVERY SENACTIV[®] SPEEDS UP MUSCLE RECOVERY BY MITIGATING INFLAMMATORY RESPONSE AFTER STRENUOUS EXERCISE^{1, 2}

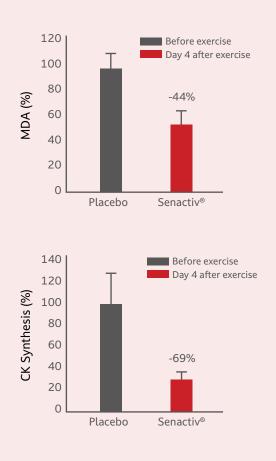
Here are the key findings demonstrated by Senactiv[®]:

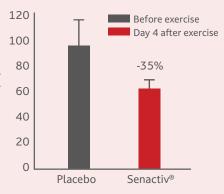
- Reduces the lipid peroxidation marker TBARS by 24% after a 60-minute cycling exercise at 80% VO2 max.
- Diminishes free radical damage to muscles, as indicated by a 44% decrease in MDA synthesis on day 4 following weight lifting exercise.
- Contributes to reduced inflammation by decreasing IL-6 synthesis by 35% on day 4 after weight lifting exercise.
- Reduces Creatine Kinase (CK) levels by 69% on day 4 after weight lifting exercise, where plasma CK levels typically rise due to protein leakage from skeletal muscles into the bloodstream after vigorous exercise.

Extended exercise can lead to increased cellular membrane peroxidation, indicated by higher TBARS or MDA levels. This oxidative process could potentially disrupt the usual cellular mechanisms involved in insulin and glucose signaling on cell surfaces, as well as glycogen storage in the muscles. Senactiv® acts as a protective shield against this type of damage caused by intense physical activity, ultimately enhancing your body's ability to sustain long and demanding workouts.



SENACTIV[®] SPEEDS UP MUSCLE RECOVERY BY MITIGATING INFLAMMATORY RESPONSE AFTER STRENUOUS EXERCISE^{1, 2}





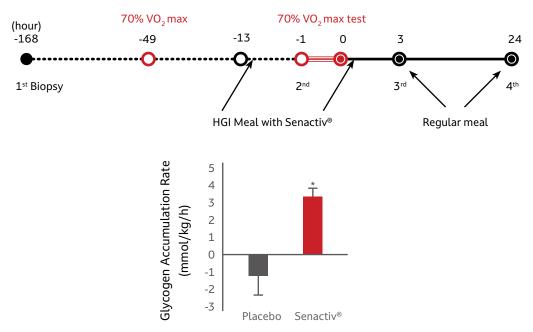
IL-6 (%)

- Hou, C.-W., Lee, S.-D., Kao, C.-L., Cheng, I.-S., Lin, Y.-N., Chuang, S.-J., ... Kuo, C.-H. (2015). Improved Inflammatory Balance of Human Skeletal Muscle during Exercise after Supplementations of the Ginseng-Based Steroid Rg1. *Plos One*, 10(1). doi: 10.1371/journal.pone.0116387
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RECOVERY SENACTIV® SPEEDS UP MUSCLE RECOVERY BY SUPPORTING INCREASED MUSCLE GLYCOGEN SYNTHESIS¹

In a study involving 14 healthy male subjects, an acute 60-minute cycling session at 70% of their VO2 max was performed. Vastus lateralis muscle samples were collected both immediately after the exercise (0 hours) and three hours postexercise. The purpose of these samples was to assess the rate of glycogen storage.

The study found that when taking Senactiv[®] both the night before and immediately after a glycogen-depleting exercise, the rate of glycogen accumulation at the three-hour mark showed a significant increase of 2.73-fold.

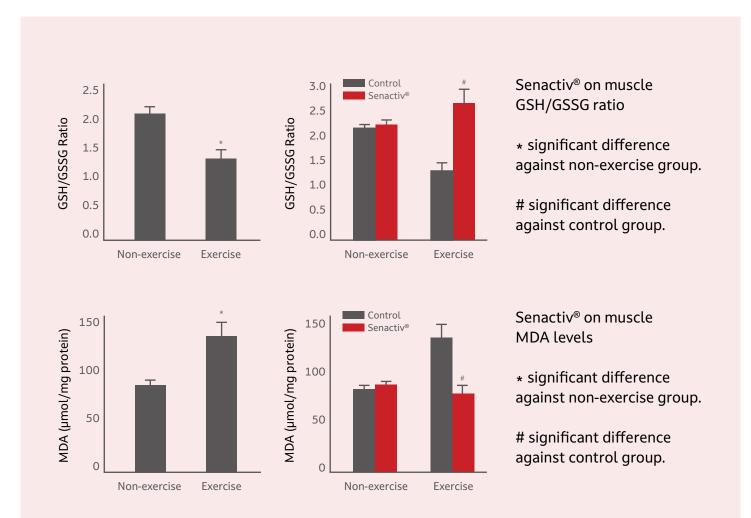


Study Design on Senactiv[®]'s Glycogen Recovery Rate in Muscles After Exercise

Muscle glycogen is the primary energy source for demanding physical activities. Senactiv® demonstrated increased glycogen re-synthesis rates by 373% following just one hour of cycling at 70% VO2 max. This 2.73-fold boost translates into enhanced recovery from fatigue, benefiting both aerobic and anaerobic activities. This effect is believed to stem from Senactiv® elevating Adiponectin secretion, subsequently influencing glucose absorption through AMPK-GLUT4 pathways within muscle cells. In essence, Senactiv® seems to optimize energy utilization in muscles, making it a promising addition for athletes

Hou, C.-W., Lee, S.-D., Kao, C.-L., Cheng, I.-S., Lin, Y.-N., Chuang, S.-J., ... Kuo, C.-H. (2015). Improved Inflammatory Balance of Human Skeletal Muscle during Exercise after Supplementations of the Ginseng-Based Steroid Rg1. *Plos One*, 10(1). doi: 10.1371/journal.pone.0116387

RECOVERY SENACTIV® REDUCES INFLAMMATION IN EXHAUSTED EXERCISE-INDUCED SARCOLEMMA LIPID PEROXIDATION IN RATS³



Exercise-induced oxidative stress temporarily induces lipid peroxidation in cell membranes, evidenced by elevated MDA levels. Senactiv® supplementation, showed potential to shield this oxidative damage by preserving the GSH/ GSSG ratio. Maintaining sarcolemma integrity holds significance as it directly impacts transmembrane glucose transport and the integrity of normal insulin signaling, which plays a pivotal role in initiating muscle glycogen synthesis.

Yu, S.-H., Huang, H.-Y., Korivi, M., Hsu, M.-F., Huang, C.-Y., Hou, C.-W., ... Kuo, C.-H. (2012). Oral Rg1 supplementation strengthens antioxidant defense system against exercise-induced oxidative stress in rat skeletal muscles. *Journal of the International Society of Sports Nutrition*, 9(1), 23. doi: 10.1186/1550-2783-9-23

CELL RENEWAL SENACTIV[®] ELIMINATES SENESCENT MUSCLE CELLS²

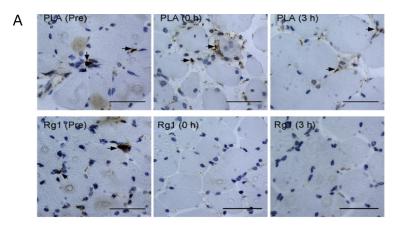
- Decreases SA-β-gal, a biomarker of senescent cell*
- Reverses apoptotic DNA fragmentation, a key feature of apoptosis*
- Reverses leukocyte infiltration in muscle faster*
- Increase in iNOS mRNA expression in muscle suggests an enhanced phagocytic function of macrophage*
- Increase in IL-6 mRNA expression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

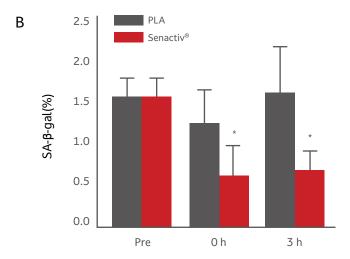
*In vastus lateralis after a 60 min cycling at 70% VO₂max

Wu, J., Saovieng, S., Cheng, I.-S., Liu, T., Hong, S., Lin, C.-Y., ... Kuo, C.-H. (2018). Ginsenoside Rg1 supplementation clears senescence-associated β-galactosidase in exercising human skeletal muscle. *Journal of Ginseng Research*. doi: 10.1016/j.jgr.2018.06.002

CELL RENEWAL SENESCENCE-ASSOCIATED β-GALACTOSIDASE (SA-β-GAL) IN HUMAN MUSCLE AFTER EXERCISE

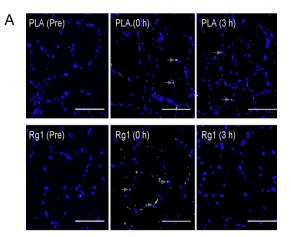
- (A) Representative immunohistochemical staining images showing SA- β -gal (brown stain indicated by arrows) in vastus lateralis muscle of a participant.
- (B) Senactiv[®] supplementation 1 h before exercise decreases SA- β -gal in vastus lateralis muscle after a 1 h cycling at 70% VO₂max.

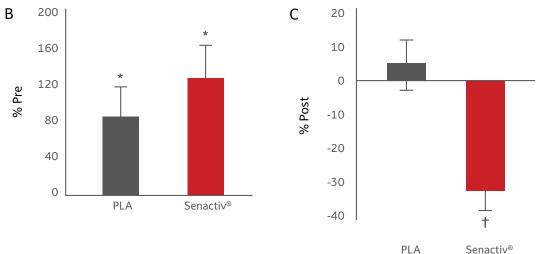




CELL RENEWAL **APOPTOTIC DNA FRAGMENTATION** IN HUMAN MUSCLE AFTER EXERCISE

- (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 Senactiv[®] trials.
- (C) Senactiv[®] supplementation 1 h before exercise reverses apoptotic nuclei in vastus lateralis muscle during a 3 h recovery.

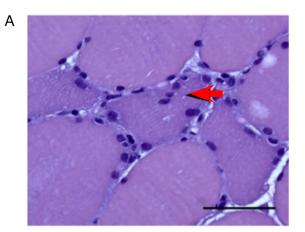


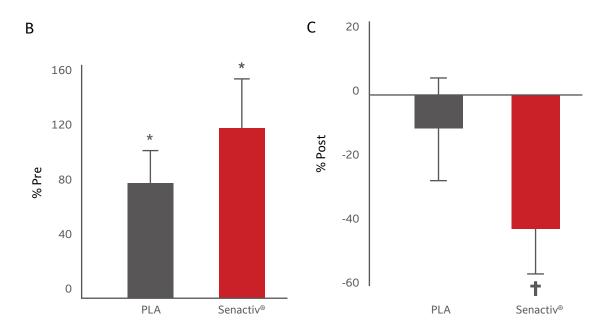


Senactiv®

CELL RENEWAL LEUKOCYTE INFILTRATION IN HUMAN MUSCLE AFTER EXERCISE

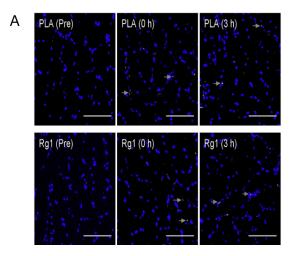
- (A) Representative hematoxylin and eosin staining images showing leukocyte infiltration (arrow) in vastus lateralis muscle cross-section of a participant.
- (B) Leukocyte infiltration increases after exercise in both PLA and Senactiv[®] trials.
- (C) Leukocyte infiltration reverses faster during a 3 h recovery in the Senactiv[®] trial compared against the PLA trial.

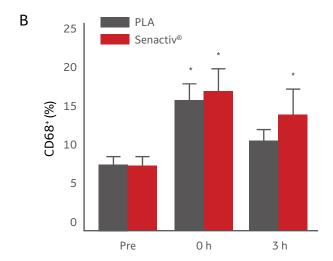




CELL RENEWAL CD68+ MACROPHAGE INFILTRATION IN HUMAN MUSCLE AFTER EXERCISE

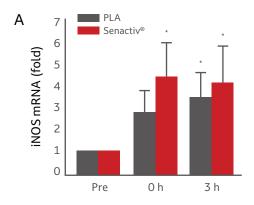
- (A) Representative immunofluorescence staining images showing CD68+ cells (green) in vastus lateralis muscle cross-section.
- (B) CD68+ macrophage increases after 1 h cycling at 70% VO₂max during both PLA and Senactiv[®] trials.

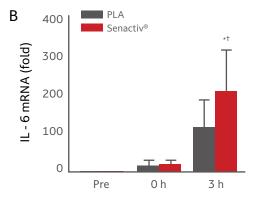


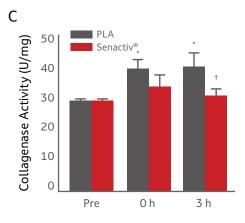


CELL RENEWAL INDUCIBLE NITRATE OXIDE SYNTHASE (INOS) AND INTERLEUKIN 6 (IL-6) MRNA LEVELS IN HUMAN MUSCLE AFTER EXERCISE

- (A) iNOS mRNA level in vastus lateralis shows an earlier increase during the Senactiv[®] trial.
- (B) IL-6 mRNA level increases after exercise in both PLA and Senactiv[®] trials. During a 3 h recovery, this increase is further amplified, to a greater extent, for the Senactiv[®] trial above the PLA trial.
- (C) Collagenase activity increases after exercise only in the PLA trial. Collagenase activity is lower in the Senactiv[®] trial, compared with the PLA trial after a 3 h post-exercise recovery.







CELL RENEWAL SENACTIV® IMPROVES ENDURANCE/STAMINA AND RECOVERY BY ACCELERATING THE REPAIR AND REGENERATION OF EXERCISING SKELETAL MUSCLES

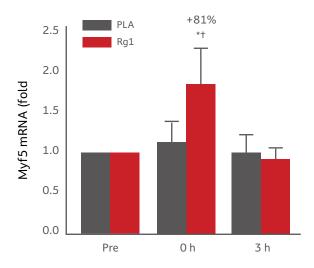
When you push your limits with endurance or high-intensity workouts, the toll on your muscles can be significant. However, the process of muscle damage triggers a sophisticated mechanism of repair, growth, and recovery. The catalyst for this transformation lies in the activation of the Pax-7 and Myf5 genes, orchestrating the activation, proliferation, differentiation, and nucleus fusion of satellite cells—an integral aspect of bolstering muscle resilience.

In a study published in the Journal of Functional Foods, Senactiv[®] demonstrated an 81% increase in Pax-7 and Myf5 gene expression. This upsurge led to heightened satellite cell activity, proliferation, differentiation, and their fusion into existing muscle tissue—an observation substantiated by the increased presence of centrally-nucleated muscle cells. This accelerated process of myogenesis in exercising skeletal muscles offers a compelling explanation for the improvements in high-intensity endurance performance associated with Senactiv[®].

Wu, J., Saovieng, S., Cheng, I.-S., Jensen, J., Jean, W.-H., Alkhatib, A., ... Kuo, C.-H. (2019). Satellite cells depletion in exercising human skeletal muscle is restored by ginseng component Rg1 supplementation. *Journal of Functional Foods*, 58, 27–33. doi: 10.1016/j.jff.2019.04.032

CELL RENEWAL SENACTIV[®] INCREASES MYF5 MRNA EXPRESSION OF HUMAN SKELETAL MUSCLE IMMEDIATELY AFTER 60 MIN CYCLING (70% VO₂MAX) BY 81%⁵

Senactiv[®] was shown in a randomized double-blind placebo-controlled crossover human clinical trial⁵ to increase the Myf5 mRNA expression by 81% immediately after a 60 min cycling exercise at 70% VO₂max. Induction of Myf5 mRNA expression is generally regarded as a hallmark for commitment of myogenesis.

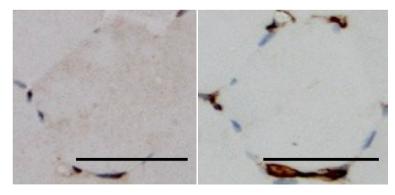


Myf5 mRNA in exercising human skeletal muscle. Expression levels are normalized to baseline (Pre). Values are expressed as means±SE (N=12). *Significantly different from baseline (Pre), P<0.05. †Significantly different from PLA, P>0.05. PLA:Placebo.

Wu, J., Saovieng, S., Cheng, I.-S., Jensen, J., Jean, W.-H., Alkhatib, A., ... Kuo, C.-H. (2019). Satellite cells depletion in exercising human skeletal muscle is restored by ginseng component Rg1 supplementation. *Journal of Functional Foods*, 58, 27–33. doi: 10.1016/j.jff.2019.04.032

CELL RENEWAL SENACTIV® DECREASES SENESCENT CELLS AND TRIGGERS CELL RENEWAL AND GROWTH TO INCREASE PHYSICAL FITNESS AND LONGEVITY

Regular physical activity promotes improved physical fitness by reducing the aged cell population in the body, leading to tissue renewal. Exercise triggers a temporary inflammation response in challenged tissues, which acts as a natural mechanism to eliminate unhealthy cells and initiate regeneration. Recent research6, highlights a decrease in p16^{INK40+} senescent cells, along with CD68+ macrophage infiltration in skeletal muscle following resistance exercise, supporting this concept. A reduced proportion of senescent cells in capillaries may contribute to enhanced physical fitness and longevity.



a. p16^{INK4a+}

b. CD34+

Senescent stem cells in capillaries surrounding myofibers of human skeletal muscle from healthy young men aged ~20 years. Representative serial immunohistochemical staining image a indicates that the detected senescent cells ($p16^{INK4a+}$) are mostly stem cells ($CD34^+$). Image B located in capillaries of human skeletal muscle.

Kuo, C.-H. (2019). Exercise Against Aging: Darwinian Natural Selection Among Fit and Unfit Cells Inside Human Body. *Journal of Science in Sport and Exercise*, 1(1), 54–58. doi: 10.1007/s42978-019-0002-y

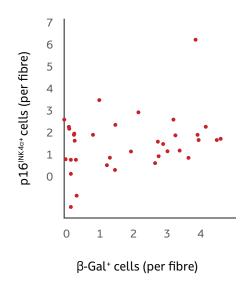
CELL RENEWAL SENACTIV® SUPPORTS THE INFLAMMATORY RESPONSE (PRE-CONDITIONING) FOR AN EARLY RESOLUTION OF THE EXERCISE STRESS RESPONSE.

A recent study published in the journal, Aging⁷, demonstrates Senactiv[®] promoting a protective mechanism for maintaining genetic stability of replicable cells against aerobic exercise.*

 $p16^{INK4\alpha}$ is a cellular senescence and oxidative stress-sensitive protein that is only detected in senescent cells. $p16^{INK4\alpha}$ induces macrophage phagocytosis to clear senescent cells in muscle and stimulate tissue repair during inflammation.

Senactiv[®] has demonstrated in a 60-minute 70% VO2max cycling exercise human trial to reduce p16^{INK4a} near to baseline 3 hours after the exercise compared to a +21-fold increase in the placebo group. This effect on p16^{INK4a} indicates the clearance of senescent cells.

Senactiv[®] also demonstrated to decrease IL-10 mRNA, an anti-inflammatory biomarker, 3-fold 3 hours after exercise, indicating the cease of macrophage phagocytosis or the absence of senescent cells after exercise.



7. Kuo, et al. (2020). Aerobic exercise induces tumor suppressor p16ink4a expression of endothelial progenitor cells in human skeletal muscle. *Aging* 12(16).

DOSAGE

PLEASE

50MG SENACTIV®

SENACTIV® IS GRAS/NDI SELF-AFFIRMED

Senactiv[®] received US GRAS/NDI self-affirmation in April, 2015 from AIBMR, Washington, USA. The affirmation was based on the 28-day Repeated 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.

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Korivi, M., Hou, C.-W., Huang, C.-Y., Lee, S.-D., Hsu, M.-F., Yu, S.-H., ... Kuo, C.-H. (2012). Ginsenoside-Rg1 protects the liver against exhaustive exercise-induced oxidative stress in rats. *Evidence-Based Complementary and Alternative Medicine*, 2012, 1–8. doi: 10.1155/2012/932165

Kuo, C.-H. (2019). Exercise against aging: Darwinian natural selection among fit and unfit cells inside human body. *Journal of Science in Sport and Exercise*, 1(1), 54–58. doi: 10.1007/s42978-019-0002-y

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Kuo, et al. (2020). Aerobic exercise induces tumor suppressor p16ink4a expression of endothelial progenitor cells in human skeletal muscle. *Aging* 12(16).

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