

Wellness Foods & Supplements

The European magazine for active ingredients

- Gut-heart axis
- Natural extracts
- Oils
- Women's health
- Vitamins
- Beauty from within





Photo®: Adobe Stock/NVBiz

Exploring Robuvit®'s mechanisms of action

Dr. Franziska Weichmann

Oak trees have long been cherished for their wood, used in building shelters, crafting boats, and producing barrels. Recently, scientists have discovered that these majestic trees also contain valuable molecules that benefit human health.

Robuvit® French oak wood extract has demonstrated impressive efficacy in human clinical studies across four key areas. First, it boosts energy levels, providing a natural way to enhance vitality. Second, it supports detoxification and liver function, aiding the body's natural cleansing processes. Third, Robuvit® significantly aids in recovery, reducing fatigue and alleviating stress, making it an excellent supplement for overall well-being. Lastly, it promotes muscle mass and improves sports performance, helping athletes achieve better results and maintain physical fitness. These benefits make Robuvit® a valuable addition to health and wellness regimens.

4 IMPRESSIVE BENEFITS



ENERGY



MUSCLE MASS AND
SPORT PERFORMANCES



DETOXIFICATION
AND LIVER FUNCTION

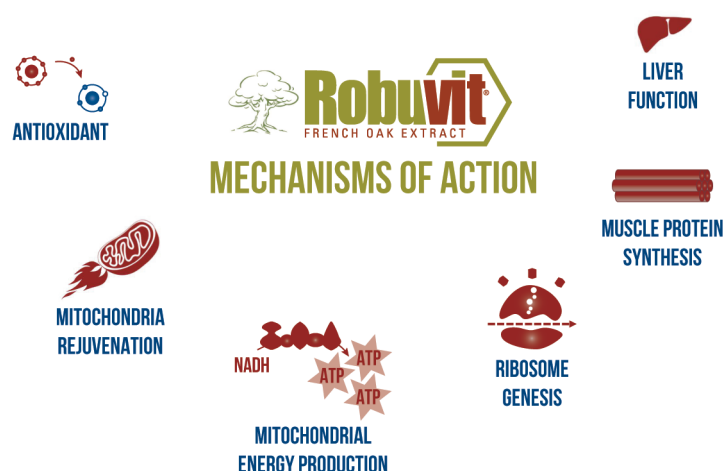


RECOVERY,
FATIGUE, STRESS

The underlying mechanisms of action for Robuvit® have been widely studied in *in vitro*, *in vivo* trials as well as gene expression studies. Clinical studies highlight Robuvit®'s powerful antioxidant proper-

ties, which protect cells from oxidative stress, contributing to overall health. Additionally, Robuvit®'s effects on mitochondrial rejuvenation and mitochondrial respiratory chain optimize ATP generation, the cellular source of energy. Increased ribosome genesis, induced by Robuvit® intake is tightly connected to optimized protein production and leads to improved cellular functionality. Urolithins, the gut metabolites of ellagitannins found in Robuvit®, show beneficial effects on muscle tissue synthesis, energy levels and liver function.

Further clinical and mechanistic studies are underway to continuously expand the knowledge surrounding Robuvit®.



Increased energy and reduced fatigue and stress

Robuvit® polyphenols, specifically ellagitannins, when ingested, undergo metabolism by gut microbiota, resulting in the generation of urolithins A, B, and C and subsequent absorption into the blood stream (1, 2). These metabolites demonstrated impressive effects on different body functions and their levels in the blood have shown to increase after oral intake of Robuvit® (1, 2).

One of these metabolites, urolithin A has been observed to promote enhanced energy production through a process called mitophagy (3). Mitophagy is a biological mechanism in which inefficient mitochondria are degraded and replaced with new and more efficient ones (4). Mitochondria are known as the powerhouses of cells and responsible for producing cellular energy in the form of ATP molecules. The process of mitophagy thus ensures optimal energy generation from consumed food and healthy functioning cells (4). In addition, Robuvit® supplementation has been shown to increase the expression of mitochondrial protein NADH-dehydrogenase, which plays a direct role in the cellular respiratory chain, further enhancing ATP generation and energy production (1).

As the intake of Robuvit® leads to improved energy output, several clinical studies have been performed to investigate the effects of Robuvit® on people with different energy deficiency issues. These

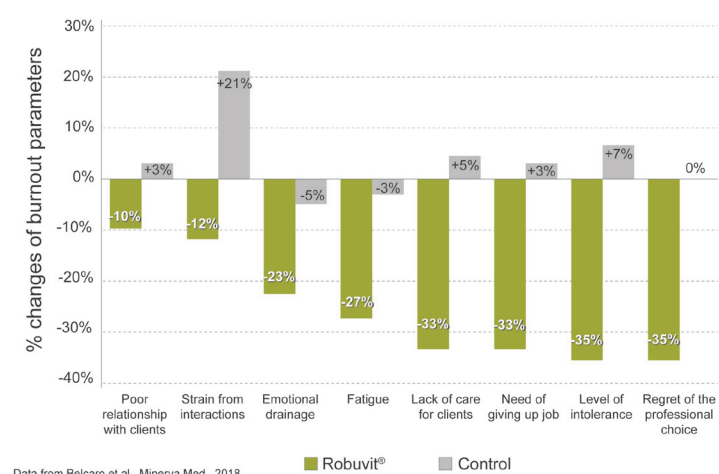
studies have shown that Robuvit® can reduce fatigue (5-7) and enhance sleep quality (5, 8, 9) in individuals with chronic fatigue syndrome, insomnia or after chemotherapy. In addition, Robuvit® led to faster recovery from conditions such as liver damage, kidney dysfunction, mononucleosis, mild heart failure, or PTSD (10-17) and post-surgery recovery (2, 18). Moreover, clinical studies showed that Robuvit® alleviates symptoms related to burn-out and work-related stress (19, 20) and boosts overall energy levels in healthy subjects (21-23).

The earliest study attributing energizing properties to Robuvit® supplementation was carried out with 20 healthy volunteers aged 45 to 65 years (21). Fatigue and energy were assessed with the "activation-deactivation, twenty item rating scale". The questionnaire provided participant's energy level based on four categories: "energy", "calmness", "tiredness" and "tension". Four weeks supplementation with Robuvit® significantly improved the energy and calm mood of subjects, and significantly reduced the fatigue and stress score of study participants (21).

A double-blind placebo-controlled study investigated the effects of Robuvit® on patients, recovering from hysterectomy, the surgical removal of the uterus (18). The participating women started the supplementation three days after surgery. After four weeks, general and mental health were significantly better in the Robuvit® group compared to placebo controls by 18 and 12%, respectively. The energy levels in the Robuvit® group increased by 3%, whereas the placebo group experienced a 10% decrease. The investigators suggested that Robuvit® can be used to relieve post-operative general and mental symptoms.

A 6-week study investigated the effects of Robuvit® on the recovery after chemotherapy for colon cancer (7). Robuvit® supplementation significantly improved patient's quality of life, mood, hand grip strength and treadmill fitness test score compared to controls. In addition, the fatigue score after six weeks was significantly reduced by 70% with Robuvit® in comparison to controls.

Robuvit® improves burnout symptoms over 4 weeks in senior professionals



In another study, Robuvit® was given to people suffering from burnout syndrome due to particularly stressful circumstances (19). The study comprised surgeons in training as well as senior professionals and managers. Their burnout symptoms were assessed by a questionnaire, including satisfaction at work, level of intolerance, emotional drainage and fatigue. After four weeks of daily Robuvit® intake, the burnout symptoms were significantly relieved in comparison with the control participants.

Muscle mass and enhanced sports performance

Urolithin B, another metabolite found in blood following Robuvit® intake, has been shown to have stimulating effects on skeletal muscle mass (24). It acts as a regulator by inducing muscle growth, increasing protein synthesis, (24). An increase in muscle mass contributes to enhanced metabolism and increased energy expenditure.

Research studies have shown that urolithin B promotes growth and differentiation of muscle cells by increasing muscle protein synthesis and repressing protein degradation (24).

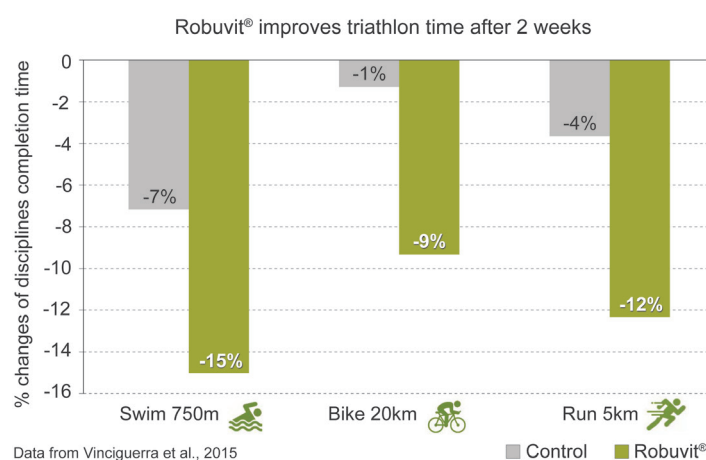
In vivo experiments confirmed the ability of urolithin B to induce muscle growth and reduce muscle tissue decrease after sciatic nerve section (24).

Furthermore, Robuvit® intake has been linked to improved protein production due to increased ribosome biogenesis (1). Ribosomal biogenesis is the vital process for protein synthesis and cellular functionality.

These findings suggest that Robuvit® has the potential to strengthen the body's adaptive response to challenging situations by providing an appropriate amount of proteins and to enhance physical endurance and fitness. In subsequent clinical studies, improved performance during sportive activities, such as triathlon or trekking was observed after Robuvit® supplementation (22, 25, 26).

Fifty-four recreational athletes in their thirties trained together for a triathlon for two weeks (25). Half of them took Robuvit® every day, the other half was assigned to a control group. After the two-week training and supplementation phase, a performance increase was seen in all subjects in the triathlon. The time needed for the respective disciplines was significantly reduced in the Robuvit® group, as compared to the control group: 12.35 minutes for swimming (-15 % vs baseline), compared to 13.18 minutes in the control group (-7 %), 34.04 minutes for biking (-9 %), compared to 35.73 minutes in the control group (-1 %) and 23.47 minutes for running (-12 %) compared to 24.63 minutes in the control group (-4 %). In addition, both muscle pain and post-performance cramping were significantly lower in the Robuvit® group compared to the control group. The time to fully recover was reduced by 10.4 % with Robuvit® compared to the controls. Interestingly, lactate dehydrogenase and unconjugated

bilirubin were significantly increased after performance in the control group, but not in the Robuvit® group. These markers of hemolysis hint to an exercise-intensified oxidative stress, which was kept at bay with Robuvit® supplementation (25, 27).



Oxidative stress can also influence ribosome biogenesis (1), potentially leading to cardiovascular, neurodegenerative, and skeletal disorders (28). Given that Robuvit® not only stimulates ribosome biogenesis but also exhibits antioxidative effects (1, 18, 23, 29), more effective and rapid abilities of the body to adapt to challenging situations result from Robuvit® intake. Clinical studies have shown several effects of Robuvit® on oxidative stress by lowering plasma oxidative stress and by increasing the levels of antioxidant enzymes (1, 18, 23, 29).

A one-month clinical study involving 20 healthy volunteers investigated the antioxidant potential of Robuvit® (29). The results showed a significant decrease of advanced protein oxidation products in the blood by more than 40 % and lipid peroxides by more than 20 % (29). This shows that Robuvit® protects proteins and lipids from oxidation. Moreover, the study revealed that Robuvit® supplementation significantly stimulated the presence of enzymes that protect the cells from oxidative attack, such as superoxide dismutase and catalase (29). Finally, Robuvit® significantly increased the plasma antioxidant capacity assessed by the FRAP (Ferric Reducing Ability of Plasma) assay. These findings suggest that Robuvit® can reduce oxidative stress and enhance the body's antioxidant defenses. Interestingly, the study also found that the effects of Robuvit® persisted even after suspending its intake. Two weeks after discontinuation of Robuvit® supplementation, the levels of oxidized proteins and lipid peroxides remained significantly lowered (29). This indicates a lasting impact of Robuvit® on oxidative stress markers.

Another double-blind, placebo-controlled study in patients recovering from surgery confirmed the antioxidant effects of Robuvit® (18). After four and eight weeks, the levels of oxidized proteins and lipid peroxides were significantly lower in the Robuvit® group compared to the placebo group (18). This supports the previous findings and further validates the antioxidant properties of Robuvit®.

Supported liver function and detoxification

The third gut metabolite found in blood following Robuvit® intake, urolithin C has been the subject of research regarding its potential on liver health. Urolithin C was investigated to be an inhibitor of liver pyruvate kinase. Inhibition of liver pyruvate kinase could be beneficial for halting or reversing non-alcoholic fatty liver disease (1, 30, 31).

In an experimental study, oral administration of urolithin C showed protective effects against liver damage and improved various markers of non-alcoholic fatty liver disease (32). The study suggests that the activation of the hepatic AMPK (AMP-activated protein kinase) signaling pathway plays a role in the beneficial effects of urolithin C on non-alcoholic fatty liver disease (32).

Liver cells possess the highest concentration of mitochondria in the human body and mitochondrial dysfunction has been involved in liver injury, including alcoholic and nonalcoholic fatty liver disease and liver inflammation (33). Thus, Robuvit®'s enhancing effects on mitochondrial function and its ability to inhibit liver pyruvate kinase contribute to overall liver health, which was shown in clinical studies (10, 11, 17).

In a three-month clinical study, Robuvit® was found to improve liver function and help prevent liver fibrosis progression in people with early symptomless hepatic damage from non-alcoholic fatty liver disease (17). The increased serum levels of two markers for non-alcoholic fatty liver disease, decreased significantly with Robuvit® compared to controls. Platelet count and albumin levels improved significantly with Robuvit® in comparison to controls. The risk for liver fibrosis decreased significantly with Robuvit® supplementation compared to controls, according to the decreased APRI (Aspartate Transaminase to Platelet Ratio) Index. After Robuvit® supplementation, the liver ultrasound characterization showed a significant decrease in the size of the liver and a lower echogenicity, representing less fibrotic changes.

Another “detox effect” could be observed after supplementation with Robuvit® in several studies: an amelioration of lymph drainage (34-37). The mechanism of action for this effect is not yet fully elucidated but the antioxidative properties of Robuvit® have beneficial impacts in this context, as high oxidative stress, enhanced formation of reactive oxygen species and accelerated lipid peroxidation processes are present in chronic lymphedematous tissue (38).

The effects of Robuvit® on early lymphatic disease were investigated in a study with 32 women (36). Robuvit® intake led to decreased leg volume by 16.4±1.1 % compared to a decrease by 9.3±1 % in controls after 4 weeks. In addition, the edema score, the interstitial fluid/plasma protein concentration ratio, limb size and ankle circumference decreased significantly with Robuvit® in comparison to controls. These effects show Robuvit®'s potent efficacy for improved detox activities in the body.

Robuvit® French oak wood extract helps to improve energy and performance, to enhance detoxification, and to reduce fatigue. These effects were shown in clinical studies and are based on well-investigated mechanisms of action of Robuvit®. Robuvit® has been shown to have strong antioxidant activities, improve mitochondrial rejuvenation and mitochondrial respiratory chain, optimizing ATP generation, and have beneficial effects on muscle tissue synthesis and on liver health that help explain the observed health benefits.

References

1. Natella F, et al. *Journal of agricultural and food chemistry*. 2014;62(2):443-53.
2. Volpp L, et al. *Front Pharmacol*. 2020;11:74.
3. Ryu D, et al. *Nat Med*. 2016;22(8):879-88.
4. Lu Y, et al. *Theranostics*. 2023;13(2):736-66.
5. Belcaro G, et al. *Panminerva Med*. 2014;56(1):63-72.
6. Belcaro G, et al. *J Neurosurg Sci*. 2015;59(2):105-17.
7. Belcaro G, et al. *Minerva Surg*. 2023;78(4):378-84.
8. Belcaro G, et al. *J Neurosurg Sci*. 2018;62(4):423-7.
9. Hu S, et al. *Minerva Cardioangiol*. 2020;68(3):203-8.
10. Belcaro G, et al. *Minerva Med*. 2014;105(1):41-50.
11. Pellegrini L, et al. *Minerva Gastroenterol Dietol*. 2016;62(3):245-52.
12. Ledda A, et al. *Panminerva Med*. 2018;60(2):60-4.
13. Hu S, et al. *Minerva Pediatr*. 2018;70(5):425-9.
14. Belcaro G, et al. *Minerva Cardioangiol*. 2020;68(3):216-23.
15. Ippolito E, et al. *J Sports Med Phys Fitness*. 2018;58(5):678-83.
16. Belcaro G, et al. *Minerva Med*. 2018;109(5):363-8.
17. Belcaro G, et al. *Minerva Gastroenterol (Torino)*. 2022;68(4):434-41.
18. Ferianec V, et al. *Nutrients*. 2020;12(4):913.
19. Belcaro G, et al. *Minerva Med*. 2018;109(3):211-7.
20. Belcaro G, et al. *Minerva Med*. 2022;113(3):518-25.
21. Országhová Z, et al. *Phytother Res*. 2015;DOI: 10.1002/ptr.5368.
22. Belcaro G, et al. *Minerva Med*. 2023.
23. Ledda A, et al. *Panminerva Med*. 2020;62(3):131-4.
24. Rodriguez J, et al. *J Cachexia Sarcopenia Muscle*. 2017;8(4):583-97.
25. Vinciguerra MG, et al. *Minerva Cardioangiol*. 2015;63(5):403-9.
26. Belcaro G, et al. *Minerva Med*. 2018;109(6):451-6.
27. Lippi G, et al. *Annals of Translational Medicine*. 2019;7(12):270-.
28. Pelava A, et al. *Biochem Soc Trans*. 2016;44(4):1086-90.
29. Horvathova M, et al. *Oxidative medicine and cellular longevity*. 2014;2014:639868.
30. Battisti UM, et al. *Pharmaceuticals*. 2023;16(5):668.
31. Battisti UM, et al. *Nutrients*. 2023;15(3):577.
32. Xu J, et al. *Naunyn Schmiedeberg's Arch Pharmacol*. 2023;396(10):2687-99.
33. Middleton P, et al. *Therap Adv Gastroenterol*. 2021;14:17562848211031394.
34. Belcaro G, et al. *Int J Angiol*. 2015;24(1):47-54.
35. Belcaro G, et al. *Minerva Chir*. 2018;73(3):288-94.
36. Hu S, et al. *Panminerva Med*. 2023;65(1):91-2.
37. Hu S, et al. *Minerva Cardioangiol*. 2020;68(3):197-202.
38. Siems WG, et al. *Qjm*. 2002;95(12):803-9.

For more information, please contact

Dr. Franziska Weichmann,
Manager of Scientific Communications
and Product Development at
Horphag Research
www.pycnogenol.com