Resveratrol SAP

Science-based antioxidant support

Resveratrol is a polyphenol that is well-known for its antioxidant, anti-inflammatory and antimicrobial properties. It is commonly found in red wine, berries, peanuts, and grape seed and skin. The numerous benefits of resveratrol have been tested in preclinical studies for a long time, and recent clinical trials have helped translate these findings into therapeutic applications. The anti-inflammatory effect of resveratrol has been found to be useful in conditions such as type-2 diabetes and polycystic ovary syndrome (PCOS). Clinical trials conducted with type-2 diabetic patients have shown that resveratrol has an anti-inflammatory effect and can also improve insulin sensitivity and glucose levels. In PCOS patients, resveratrol can help improve inflammation markers in granulocytes in ovaries, improve oocyte quality, and regulate the menstrual cycle. Resveratrol, due to its overall beneficial effects and its antioxidant properties, is useful in other non-disease states as well. One of the major areas of research points to decrease in body weight, fat mass, waist circumference, and increase in lean mass with resveratrol intake. In addition to improving glucose, lipid metabolism, and inflammation parameters, resveratrol may help improve bone mineral density and support bone health biomarkers in postmenopausal women. Further research should help understand its applications in other bone degeneration disorders.

Resveratrol SAP provides a safe dose of high-quality natural resveratrol for antioxidant, anti-inflammatory effects and helps improve PCOS, diabetes, and bone health in postmenopausal women.

ACTIVE INGREDIENTS

Each vegetable capsule contains:
trans-Resveratrol (from Japanese knotweed (*Reynoutria japonica,* root)). . . . . 375 mg

Other ingredients: Vegetable magnesium stearate and silicon dioxide in a capsule composed of carbohydrate gum and purified water.

Contains no: Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial colours and flavours, starch or sugar.

This product is non-GMO and vegan friendly.

Resveratrol SAP contains 60 capsules per bottle.

DIRECTIONS FOR USE

Adults: See indication-specific dosages outlined in the indication-specific dosage table.

Take 1-2 capsules once daily or as directed by your healthcare practitioner.

DURATION OF USE

Consult a healthcare practitioner for prolonged use.

INDICATIONS

Resveratrol SAP can help:
- Promote healthy inflammatory response.
- Manage blood glucose levels and type-2 diabetes.
- Improve symptoms of PCOS.
- Enhance bone health.

CAUTIONS AND WARNINGS

Consult a healthcare practitioner prior to use if you are pregnant, breast-feeding, or if you are taking prescription medications as resveratrol may alter the effectiveness of these medications.

Do not use if seal is broken. Keep out of reach of children.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **Resveratrol SAP** lot number have been tested by an ISO 17025 accredited third-party laboratory for identity, potency, and purity.

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

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Resveratrol is a key polyphenolic compound well known for its antioxidant, anti-inflammatory and antimicrobial properties. Other benefits of resveratrol include action against oxidative stress, neurodegeneration, and diabetic pathophysiology. [1,2] It is found in red wine, berries, grape varieties (skin and seeds), peanuts and various other plant sources. [1] The ability of resveratrol to inhibit the production of inflammatory factors has increased its potential benefits in management of neural damage, heat induced oxidative stress, and bacterial endotoxin-related inflammation. [3] Clinical benefits of this mechanism of action are seen in management of diabetes and polycystic ovary syndrome (PCOS), where resveratrol not only helps manages inflammatory factors, but can help manage androgen levels and improve menstrual regularity. [4] There is a cohort of clinical trials that have established the supplementation of resveratrol with weight loss parameters, and some initial evidence also points to improvement in bone health biomarkers.

PCOS

Although more clinical trials need to be conducted, current data shows a clear connection between resveratrol use and management of PCOS symptoms. A randomized, double-blind, placebo-controlled trial with 30 PCOS patients showed that supplementation with 1500 mg/day of resveratrol for 3 months lowered testosterone, dehydroepiandrosterone sulfate, fasting insulin levels, and increased insulin sensitivity. [5] An improvement in menstrual cycle regularities and hair loss compared with placebo was observed with administration of 1000 mg/day of resveratrol for 3 months to 78 participants in another randomized trial. [6] The anti-inflammatory effects of resveratrol are useful in PCOS patients as well, since PCOS is an inflammatory condition characterized by endoplasmic reticulum stress. In a randomized, triple-blind placebo-controlled trial with 40 PCOS patients, inflammatory biomarkers were studied in the cumulus cells - granulosa cells that help with maturation and fertilization of oocytes. Supplementation with 800 mg/day of resveratrol for 40 days decreased levels of inflammatory biomarkers such as interleukin-6, interleukin-1β, CRP, TNF-α, and NF-κB. Gene profiling of these cells showed an increase in expression of ATF6, ATF4 (activating transcription factors), and a decrease in the expression of GRP78, CHOP, XBP1, thus demonstrating the ability of resveratrol to modulate metabolic pathways and gene expression. [7] Gene expression modification was observed in another clinical trial (n=62), where administration of 800 mg/day of resveratrol for 40 days was associated with reduced gene expression of VEGF, HIF1 gene, accompanied by lower levels of testosterone and luteinizing hormone (LH). The hormonal profile showed increase in levels of thyroid-stimulating hormone (TSH) and follicle-stimulating hormone (FSH), with increased levels of high-quality oocyte rate and high-quality embryo rate. [8] Further research should help clarify the role of resveratrol in modulating gene expression in the management of PCOS symptoms.

INFLAMMATION, DIABETES AND LIPID METABOLISM

There is a plethora of studies that have shown a clear link between resveratrol supplementation and management of lifestyle diseases. A meta-analysis of 29 randomized controlled trials (n=1069) concluded that a dose of 500 mg/day of resveratrol for 3 or more months can help reduce levels of fasting glucose, HbA1c, low-density lipoprotein cholesterol (LDL-C), diastolic blood pressure (DBP), total cholesterol and C-reactive protein (CRP). [9] The management of inflammatory markers in type-2 diabetes patients has been an especially productive area in resveratrol research. A meta-analysis of 6 randomized controlled trials (n=491) showed reduced levels of CRP in diabetic patients with average 335 mg/day dose of resveratrol for an average of 19 weeks. [10] Resveratrol appears to target specific inflammatory markers, especially CRP. A meta-analysis of 24 randomized controlled trials for high-sensitivity (hs) CRP and 11 trials for CRP showed reduced serum levels of these inflammatory markers, with an optimal effect observed at 500 mg/day with at least 10 weeks of treatment. [11] A similar approach in another meta-analysis showed a reduction in CRP and TNF-α with a dose of ≤500 mg/day used in most trials with an average duration of 4 months, with a cohort of 17 randomized controlled trials. [12] These analyses establish the anti-inflammatory effect of resveratrol in diabetic and non-diabetic people. The effect on diabetic population though is of special interest, since resveratrol also appears to improve other parameters of diabetes. A meta-analysis of 6 randomized, placebo-controlled trials (n=196) showed that an average dose of 1136 mg/day, duration 4 weeks-12 months, can help reduce levels of HbA1c and creatinine, as well as lower systolic blood pressure, when used in adjunct with conventional type-2 diabetes therapy. [13] A randomized trial conducted with 110 participants showed a reduction in plasma glucose, insulin, and insulin resistance, with reduction in inflammatory biomarkers MDA, hs-CRP, TNF-α, IL-6, at a dose of 200 mg/day for 24 weeks. Participants also showed a down regulation of associated microRNA expression, pointing to an area of further exploration for use of resveratrol as an adjunct therapy in diabetes. [14]

WEIGHT LOSS

Another area of resveratrol benefit is weight loss, an application that has been widely studied with successful results. A meta-analysis of 28 randomized controlled trials (n=1514) showed a decrease in body mass index (BMI), waist circumference (WC), and body weight with resveratrol supplementation. A dose <500 mg for ≥3 months was observed to have the most effect on body weight. [15] A different dose was recommended by another meta-analysis for weight loss, however, where a dose of ≥500 mg/day for >10 weeks was recommended for decrease of WC and glucose. This analysis also found a reduction in triglycerides and an increase in HDL in some of the 10 clinical trials it analyzed. [16] The most recent meta-analysis has taken into account 36 randomized controlled trials and observed that a dose <200 mg/day had better effect on weight loss, compared to 200-500 mg/day or >500 mg/day. The duration of supplementation was found to be more effective with >17 weeks of use. [17] The impact of resveratrol on body parameters and physiological biomarkers of glucose and lipid metabolism makes it an ideal candidate for weight loss and management of lifestyle diseases.

BONE HEALTH

A relatively new area of research regarding resveratrol is its use in improvement of bone health biomarkers. A meta-analysis of 6 randomized clinical trials (n=264) showed that supplementation with 1000 mg/day for an average of 11 weeks can increase serum alkaline phosphatase, and bone alkaline phosphatase, biomarkers of bone health. [18] Bone mineral density is a critical factor impacting the quality of life of menopausal women. A randomized, double-blind, placebo-controlled crossover trial with 125 menopausal women found that supplementation with 150 mg/day of resveratrol for 12 months significantly improved lumbar spine, neck-of-femur bone density, reduced bone reabsorption biomarkers, and decreased the probability of fractures. [19] Further research should help understand the mechanism of action of resveratrol in improving bone health, thereby expanding its applications.

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For healthcare professional use only.

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NFH®

INDICATION SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety have been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias etc) assessed and have been rated using a 5 star ★ rating classification.

Indication	Suggested dosage	Supporting evidence and study outcomes	Study design	Outcomes measures/ selection criteria for studies	Safety	Evidence quality rating
Inflammation and Diabetes Clinical Markers						
Inflammation (CRP and hs-CRP)[1]	2 capsules/day for at least 10 weeks	Reduced serum hs-CRP and CRP	Randomized controlled trials - 24 for hs-CRP, 11 for CRP, (n=1741) dose 8-100 mg/day (optimal effect at ≥500 mg/day for ≥10 weeks duration)	Serum levels of CRP and hs-CRP	Mild gastrointestinal effects may be observed	★★★★★
CRP in type-2 diabetes patients[2]	1 capsule/day for 19 weeks	Reduced levels of CRP in participants with type-2 diabetes	6 Randomized controlled trials (n=491), dose average of 335 mg/day and duration average of 19 weeks	Levels of CRP	No adverse effects	★★★★★
Inflammatory markers (CRP and TNF-α)[3]	2 capsules/day for 16 weeks	Reduced levels of TNF-α and hs-CRP	17 randomized controlled trials (n=736), dose ≤500 mg/day used in most trials with an average duration of 4 months	Levels of inflammatory markers (CRP, IL-6 and TNF- α	No adverse effects	★★★★★
Glycemic control, inflammation, oxidative stress[4]	1 capsule/day for 24 weeks	Reduction in plasma glucose, insulin and insulin resistance, MDA, hs-CRP, TNF- α, IL-6. Down-regulation of associated microRNA expression	Randomized, double-blind, placebo-controlled trial (n=110), dose 200 mg/day for 24 weeks	Fasting glucose, insulin, HbA1c, lipid profile, TNF- α, IL-6, hs-CRP, MDA (inflammatory markers), circulatory micro-RNAs	No adverse events	★★★★★
Reduction of risk factors of non-communicable diseases[5]	2 capsules/day for 12 weeks	Reduced levels of fasting glucose, HbA1c, LDL-C, DBP, total cholesterol, CRP	29 Randomized controlled trials (n=1069) dose of 500 mg/day with duration of ≥3 months suggested	Fasting glucose, total cholesterol, C-reactive protein, blood pressure, lipid biomarkers	No adverse events	★★★★★
Adjunct to type-2 diabetes therapy[6]	3 capsules/day for minimum 4 weeks	Reduced levels of SBP, HbA1c and creatinine	6 Randomized, placebo-controlled trials (n= 196), dose avg. 1136 mg/day, duration 4 weeks-12 months	SBP, HbA1c, creatinine, fasting glucose, insulin resistance, DBP, triglycerides, LDL, HDL	No adverse events	★★★★★
Weight Loss						
Weight loss[7,8]	1 capsule/day for >17 weeks	Decreased body weight, BMI, fat mass, waist circumference. Increase in lean muscle mass	36 Randomized, placebo-controlled trials (n=1560), dose <200 mg/day showed better weight loss than 200-500 mg/day or >500 mg/day. Duration- effect better with >17 weeks of use 28 Randomized, placebo-controlled trials (n=1514), dose <500 mg for ≥3 months appeared to have the most effect on body weight	leptin, and adiponectin levels, BMI, fat mass, lean mass body weight, and waist circumference, body weight, waist circumference, fat mass, BMI	No adverse events	★★★★★
Weight loss and metabolic syndrome[9]	2 capsules/day for >10 weeks	Reduced waist circumference, body weight, triglycerides, glucose, and increased HDL	10 Randomized, placebo-controlled trials (n=396), dose of ≥500 mg/day for >10 weeks recommended for decrease of waist circumference and glucose	Waist circumference, body weight, triglycerides, glucose, HDL	No adverse events	★★★★★
PCOS						
Androgen levels[10]	4 capsules/day for 12 weeks	Decrease in testosterone, dehydroepiandrosterone sulfate, fasting insulin level and increase in insulin sensitivity	Randomized, double blind, placebo-controlled trial (n=30), dose 1500 mg/day for 3 months	Testosterone, dehydroepiandrosterone sulfate, insulin, insulin sensitivity, gonadotropins, lipid profile, inflammation and endothelial function markers	No adverse events	★★★★★
PCOS improvement[11]	2 capsules/day for 40 days	Reduced gene expression of VEGF, HIF1 genes, lower levels of testosterone and LH. Increase in TSH and FSH levels. Higher levels of high-quality oocyte rate and high-quality embryo rate	Randomized, triple-blind, placebo-controlled trial (n=62), dose 800 mg/day for 40 days	FSH, LH, TSH, VEGF, HIF1 gene expression, number of mature oocytes, fertilization rate, cleavage rate, fertility rate	No adverse events	★★★★★

Anti-inflammatory effects in PCOS patients[12]	2 capsules/day for 40 days	Decreased levels of inflammatory biomarkers. Increase in expression of ATF6 and ATF 4, decrease in expression of GRP78, CHOP, XBP1	Randomized, triple-blind, placebo-controlled trial (n=40), dose 800 mg/day for 40 days	Gene expression in cumulus cells- ATF4, ATF6, CHOP, GRP78, and XBP1s. Levels of IL-6, IL-1β, IL-18, TNF-α, NF-κB, and CRP	No adverse events	★★★★★
Menstrual cycle regulation and hair loss[13]	3 capsules/day for 12 weeks	Higher menstruation rate, lower hair loss	Randomized, double-blind, placebo-controlled trial (n=78), dose 1000 mg/day for 3 months	Clinical features- hirsuitism, hair loss, acne, menstruation frequency, ultrasonography. Body mass, weight, testosterone, LH, FSH, prolactin, insulin, TSH, C-peptide, lipid profile, SHBG	No major adverse events	★★★★★
Bone Health						
Bone health biomarkers[14]	3 capsules/day for 11 weeks or more	Increase in serum alkaline phosphatase, and bone alkaline phosphatase	6 Randomized clinical trials (n=264), dose of 1000 mg/day considered ideal for lowering ALP levels and the duration average was 11 weeks	Serum calcium, osteocalcin, C-terminal telopeptide of type I collagen, procollagen I N-terminal propeptide	No adverse events	★★★★★
Bone mineral density in postmenopausal women[15]	1 capsule/day for 12 months	Improvement in lumbar spine, neck of femur bone density, reduction in CTX bone reabsorption marker, reduced probability of fracture	Randomized, double-blind, placebo-controlled, two-period crossover period of 24 months (n=125) dose 150 mg/day for 12 months	Bone mineral density in lumbar spine, hip, and whole body. Plasma levels of osteocalcin, C-terminal telopeptide type-1 collagen (CTX), overall vascular function	Some adverse effects reported but could not be attributed to resveratrol intake	★★★★★

TNF-α-tumor necrosis factor-alpha, IL-interleukin, CRP-C-reactive protein, hs-CRP- high-sensitivity C-reactive protein, MDA-malondialdehyde, DBP-diastolic blood pressure, LDL-C low density lipoprotein C, SBP - systolic blood pressure, HDL - high density lipoprotein, BMI - body mass index, ALP - alkaline phosphatase, VEGF - Vascular endothelial growth factor, HIF1 – Hypoxia-Inducible Factor 1, LH - Luteinizing hormone, FSH - follicle-stimulating hormone, TSH- thyroid stimulating hormone, ATF4- Activating Transcription Factor 4, ATF6 - Activating Transcription Factor 6, CHOP - C/EBP homologous protein, GRP78 - also known as Binding immunoglobulin protein, XBP1 - X-box binding protein 1, NF -κB - nuclear factor kappa-light-chain-enhancer of activated B cells, SHBG - sex hormone binding globulin.

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