**Resveratrol’s Promising Role in Women’s Health**   
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Resveratrol is a naturally-occurring polyphenolic compound found in grapes, wine and other plant foods.1,2 As an antioxidant, resveratrol neutralizes free radicals, which are hypothesized to be associated with aging, cardiovascular disease and other inflammatory medical conditions.3,4 For this reason, resveratrol is widely used in dietary supplements for its cardiovascular, metabolic and anti-inflammatory benefits.

In recent years, scientific literature has accumulated supporting the use of resveratrol in nutritional supplements to sustain and support healthy aging — including the management of arthritis, metabolic bone disease, and osteoporosis.5,6 The potential for resveratrol to help women live better as they age by playing a role in metabolic support and health maintenance is an exciting opportunity to explore.

THE MENOPAUSAL TRANSITION

While life expectancy has been prolonged over the years, menopause occurrence has not – women may spend a third to one half of their lives in menopause.7 According to a recent survey, three quarters of women say that menopause caused them to change their life and more than half say it had a negative impact on their lives.8

As we age, our bodies experience gradual changes and decline. While most of these changes are not gender specific, in some cases these physiologic shifts are more relative for women than men. On average, when a woman approaches menopause near the age of 50, the production of estrogen, the predominant female steroid hormone, begins to decrease.7

Menopause is a normal part of aging for females and is defined as the point in time when ovaries are no longer functional and menstrual periods stop. Menopause does not always reference an immediate occurrence; rather, for some, menopause is a gradual decline and cumulative change in metabolic processes that can begin several years before the final menstrual period. This transitional stage leading up to menopause is defined as perimenopause, and can last up to 14 years.5,7-8

Decreased production of estrogen may result in a variety of symptoms associated with menopause. Women transitioning through menopause may experience a variety of symptomatic effects that may negatively impact quality of life, such as: mood changes, including depression; increased perception of pain and lowered sexual desire and activity8; loss of skin elasticity and the appearance of wrinkles and age spots14; and progressive loss of skeletal muscle mass and function.15

**Resveratrol in a healthy lifestyle regimen**

Fortunately, in the past couple of decades, awareness of these changes has increased and, in parallel, new nutritional strategies to help manage them have emerged. The inclusion of resveratrol and other polyphenols as part of healthy diet and active lifestyle may be an effective way to tackle some of these menopause-related conditions. Among the dietary interventions supporting healthy aging in women, polyphenols such as resveratrol, soy isoflavones, green tea flavonoids, curcumin and others have gained traction in the past two decades.16

The antiaging effects of resveratrol may be due to several related mechanisms, including: its antioxidant properties; potential role as a dietary phytoestrogen; and possible role in promoting mitochondrial biogenesis,17 a term that simply refers to the replication of mitochondria in the cell. As we age, our body’s ability to grow new mitochondrial cells, which drive energy production in the body, slows down.18 By promoting mitochondrial cell growth, resveratrol may help return the body’s processes to a younger state. This combination of features makes resveratrol a unique compound for anti-aging activity.

*The widespread effects of antioxidants in health science have led researchers to explore the use of resveratrol in a variety of women’s health-related applications – including bone health; muscle function; skin and metabolic health; and mood, pain and sexual activity.*

**Osteoporosis**

The delicate balance between bone formation and bone resorption degrades with aging — when bone resorption overtakes bone formation. The decrease in circulating estrogen limits the body’s ability to remodel bones and increases a postmenopausal woman’s risk of developing osteoporosis.19

The significant decrease in estrogen may cause bone loss, potentially leading to hip, spine and wrist fractures. In fact, 30% of postmenopausal women have been found to have osteoporosis.12 It is estimated that approximately one in two women older than 50 will suffer from an osteoporosis-related bone fracture.12,13

Preclinical data shows promise in the potential of resveratrol to mediate osteoporosis-related outcomes.5 Two published studies on osteoporosis have been conducted in overweight and obese men.20,21 One study showed that supplementation with Veri-te™ resveratrol leads to a significant dose-dependent increase in bone mineral density.20 Another demonstrated a dose-dependent increase in bone alkaline phosphatase (BAP),21 a biochemical marker of bone formation, stimulating mineralization and increasing bone mineral density. BAP may be a useful marker in the treatment of postmenopausal osteoporotic women.22

Tofurther elucidate the impact of resveratrol on bone health, additional clinical studies are ongoing. Of note, a current study at the University of Newcastle (Australia) lead by Peter Howe, PhD, is examining the resveratrol/bone health connection in a broader study of health in post-menopausal women.

Although it is difficult to generalize clinical research findings across sexes, both older men and women experience bone loss, yet osteoporosis is often accelerated at an earlier age in post-menopausal women. Given this earlier occurrence, the role of nutritional support with supplements such as resveratrol may be more important for women than men.

**Muscle function**   
  
The term sarcopenia refers to normal, progressive and age-related loss in muscle mass. There is a large body of evidence that supports the hypothesis that the decline in estrogen levels surrounding menopause may play a role in the development of sarcopenia in postmenopausal women.15

A randomized control trial in 30 older adults found that the combination of exercise and an oral intake of 500 mg of resveratrol per day significantly improved muscle fatigue resistance compared to the placebo group. Moreover, several parameters related to muscular function (e.g., knee extensor muscle peak torque, average peak torque and power) improved in the group receiving resveratrol, but not the group receiving the placebo. The authors concluded that results from this study may suggest that resveratrol supplementation combined with exercise may provide an enhanced approach for reversing sarcopenia than exercise alone.23

**Skin health**

As we age, our skin does, too. It no longer looks as plump and smooth, it becomes thinner, loses its firmness and can take longer to heal. What was once trouble-free skin, develops wrinkles, dark circles and age spots.24

A placebo-controlled, double-blind study involving 50 women and men (aged between 35 and 65) showed that after 60 days, supplementation with a dietary supplement blend containing 8 mg of resveratrol significantly decreased systemic oxidative stress, improved skin moisturization and elasticity, diminished skin roughness and depth of wrinkles and significantly decreased the intensity of age spots. The authors concluded that the specific resveratrol blend may be a promising strategy to reduce skin wrinkling, as well as reduce systemic and skin oxidative stress.25

**Menopause-related symptoms: mood, pain, and sexual function**

Other potential benefits of resveratrol for women’s health are related to its effects on mood, pain and sexual function. A recent clinical study in postmenopausal women showed that an oral intake of 75 mg of resveratrol twice daily for 14 weeks reduced the perception of pain and improved total well-being. Interestingly, both benefits, including measures of quality of life, correlated with improvements in cerebrovascular function. The authors concluded that the results indicated potential for resveratrol in aiding management of chronic pain associated with age-related osteoarthritis.26

Another study conducted in 60 perimenopausal women experiencing vasomotor symptoms (hot flashes) aimed to evaluate the effect of a resveratrol-containing supplement on sexual function and other menopause-related symptoms. Researchers used two questionnaires to determine the change in sexual function and sexual distress over the course of a six-month study duration. At the six-month follow-up, the sexual function score was significantly higher and the sexual distress score significantly lower compared to baseline scores. Menopause symptoms were also improved in all categories. The authors concluded that the resveratrol-containing supplement improved some perimenopausal symptoms in women and hypothesized that the improvement of the vasomotor function may contribute to the improvement of quality of life and sexual function in this population.27

**Summary**

The available research suggests that resveratrol, as a unique antioxidant and phytoestrogen, may be a promising dietary supplement to support several women’s health and menopause-related outcomes. In addition, resveratrol’s potential role in promoting mitochondrial biogenesis may help slow age-related decline at the cellular level. These functions highlight resveratrol’s role as a unique ingredient for women’s health. Furthermore, studies show that resveratrol may be a useful supplement for promotion of women’s health when combined with an overall healthy diet and active lifestyle. While the function of resveratrol as an antioxidant with anti-inflammatory properties is well known, there is an opportunity for additional research to further demonstrate the role of resveratrol to support women’s health specifically.

For more information on Veri-te™ resveratrol, visit <https://www.veriteresveratrol.com/>.

**References**

1. Soleas, G. J., Diamandis, E. P. & Goldberg, D. M. Resveratrol: A molecule whose time has come? And gone? *Clinical Biochemistry* **30,** 91–113 (1997).
2. Constant, J. Alcohol, ischemic heart disease, and the French paradox. *Clin Cardiol* **20,** 420–424 (1997).
3. Britton, R. G., Kovoor, C. & Brown, K. Direct molecular targets of resveratrol : identifying key interactions to unlock complex mechanisms. **1348,** 124–133 (2015).
4. Kulkarni, S. S. & Cantó, C. The molecular targets of resveratrol. *Biochim. Biophys. Acta - Mol. Basis Dis.* **1852,** 1114–1123 (2015).
5. Mobasheri, A. & Shakibaei, M. Osteogenic effects of resveratrol in vitro: Potential for the prevention and treatment of osteoporosis. *Ann. N. Y. Acad. Sci.* **1290,** 59–66 (2013).
6. Mobasheri, A., Henrotin, Y., Biesalski, H. K. & Shakibaei, M. Scientific evidence and rationale for the development of curcumin and resveratrol as nutraceutricals for joint health. *Int. J. Mol. Sci.* **13,** 4202–4232 (2012).
7. The American Congress of Obstetricians and Gynecologists. Women's health stats and facts. 1-56 (2011).
8. British Menopause Society. A woman's relationship with menopause is complicated. https://www.womens-health-concern.org/\_wpress/wp-content/uploads/2015/01/BMS-Infographic-10-October2017-01C.pdf (2017).
9. National Institute on Aging. What is menopause? https://www.nia.nih.gov/health/what-menopause (2017).
10. Mayo Clinic. Menopause - Symptoms and causes. https://www.mayoclinic.org/diseases-conditions/men (2017).
11. National Osteoporosis Foundation. What women need to know. https://www.nof.org/preventing-fractures/general-facts/what-women-need-to-know/ (2017).
12. National Osteoporosis Foundation (NOF) Clinician’s guide to prevention and treatment of osteoporosis (2013).
13. International Osteoporosis Foundation. Facts and Statistics. https://www.iofbonehealth.org/facts-statistics (2017).
14. Thornton, M. J. Estrogens and aging skin. *Dermatoendocrinol.* **5,** 264–270 (2013).
15. Messier, V. *et al.* Menopause and sarcopenia: A potential role for sex hormones. *Maturitas* **68,** 331–336 (2011).
16. Caroline J. Hollins Martin, Ronald Ross Watson, V. \_R. P. (Eds. . *Nutrition and Diet in Menopause*. (2013). doi:10.1007/978-1-62703-373-2
17. Csiszar, A., Labinskyy, N., Pinto, J.T., Ballabh, P., Zhang, H., Losonczy, G., Pearson, K., de Cabo, R., Pacher, P., Zhang, C., Ungvari, Z. Resveratrol induces mitochondrial biogenesis in endothelial cells. *Am J Physiol Heart Circ Physiol* **297**, H13-20 (2009).
18. Sun, N., Youle, R. J., Finkel, T. The Mitochondrial Basis of Aging*.* *Molecular Cell* **61**, 654-666 (2016).
19. Ethel S. Siris, MD; Paul D. Miller, MD; Elizabeth Barrett-Connor, MD; et alKenneth G. Faulkner, PhD; Lois E. Wehren, MD; Thomas A. Abbott, PhD; Marc L. Berger, MD; Arthur C. Santora, MD; Louis M. Sherwood, MD. Identification and Fracture Outcomes of Undiagnosed Low Bone Mineral Density in Postmenopausal Women, Results from the National Osteoporosis Risk Assessment.  *JAMA* **286***,* 2815-2822 (2001). doi:10.1001/jama.286.22.2815
20. Poulsen, M. M. *et al.* Short-term resveratrol supplementation stimulates serum levels of bone-specific alkaline phosphatase in obese non-diabetic men. *J. Funct. Foods* **6,** 305–310 (2014).
21. Ornstrup, M. J., Harsløf, T., Kjær, T. N., Langdahl, B. L. & Pedersen, S. B. Resveratrol Increases Bone Mineral Density and Bone Alkaline Phosphatase in Obese Men: A Randomized Placebo-Controlled Trial. *J. Clin. Endocrinol. Metab.* **99,** 4720–4729 (2014).
22. Nakamura, Y., Suzuki, T. & Kato, H. Serum bone alkaline phosphatase is a useful marker to evaluate lumbar bone mineral density in Japanese postmenopausal osteoporotic women during denosumab treatment. *Ther. Clin. Risk Manag.* **13**,1343-1348 (2017)
23. Alway, S. E. *et al.* Resveratrol Enhances Exercise-Induced Cellular and Functional Adaptations of Skeletal Muscle in Older Men and Women. *Journals Gerontol. Ser. A* **138,** 3657–3666 (2017).
24. National Institute on Aging. Skincare and Aging. https://www.nia.nih.gov/health/skin-care-and-aging (2017).
25. Buonocore, D. *et al.* Resveratrol-procyanidin blend: Nutraceutical and antiaging efficacy evaluated in a placebo-controlled, double-blind study. *Clin. Cosmet. Investig. Dermatol.* **5,** 159–165 (2012).
26. Wong, R., Evans, H. & Howe, P. Resveratrol supplementation reduces pain experience by postmenopausal women. *Menopause* **24,** 916–922 (2017).
27. Caruso, S. *et al.* Effects of nutraceuticals on quality of life and sexual function of perimenopausal women. *J. Endocrinol. Invest.* **40,** 27–32 (2017).