March 27, 2023

Re: Éternel: Curated Blend and Cellular Absorption Technology Clinical Dossier

Here at THREE, we provide curated proactive wellness solutions using our proprietary Cellular Absorption Technology, proven to help you live a life of greater health and purpose.

This dossier contains peer-reviewed clinical studies both on the curated blend and the Cellular Absorption Technologies used in Éternel that validates its ability to do the following:

- Protect and support cells from damage and premature aging.
- Promote cellular health and longevity.
- Work to neutralize free radicals.
- Deliver powerful phytonutrients to protect against UV damage.

One thing that you can expect from us here at THREE is that we are always in the process of running clinical studies in elucidating new mechanisms of action by which our products work along with discovering additional areas in which our products can promote human health. We have several exciting clinical studies in the pipeline and will announce these when they are completed.

The clinical studies contained herein, and others that will follow, explain why our products provide the powerful health benefits our customers from all around the world experience every time they use a THREE product.

Thank you for joining us on this journey and for trusting us with your proactive wellness needs.

Be well,

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Cells. 2022 Aug 3;11(15):2391. doi: 10.3390/cells11152391.

Açaì (*Euterpe oleracea*) Extract Protects Human Erythrocytes from Age-Related Oxidative Stress

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PMID: 35954235 PMCID: PMC9368007 DOI: 10.3390/cells11152391

Free PMC article

Abstract

Aging is a process characterised by a general decline in physiological functions. The high bioavailability of reactive oxygen species (ROS) plays an important role in the aging rate. Due to the close relationship between aging and oxidative stress (OS), functional foods rich in flavonoids are excellent candidates to counteract age-related changes. This study aimed to verify the protective role of Açaì extract in a d-Galactose (d-Gal)-induced model of aging in human erythrocytes. Markers of OS, including ROS production, thiobarbituric acid reactive substances (TBARS) levels, oxidation of protein sulfhydryl groups, as well as the anion exchange capability through Band 3 protein (B3p) and glycated haemoglobin (A1c) have been analysed in erythrocytes treated with d-Gal for 24 h, with or without pre-incubation for 1 h with 0.5-10 µg/mL Açaì extract. Our results show that the extract avoided the formation of acanthocytes and leptocytes observed after exposure to 50 and 100 mM d-Gal, respectively, prevented d-Gal-induced OS damage, and restored alterations in the distribution of B3p and CD47 proteins. Interestingly, d-Gal exposure was associated with an acceleration of the rate constant of SO_4^{2-} uptake through B3p, as well as A1c formation. Both alterations have been attenuated by pre-treatment with the Açaì extract. These findings contribute to clarify the aging mechanisms in human erythrocytes and propose functional foods rich in flavonoids as natural antioxidants for the treatment and prevention of OS-related disease conditions.

Keywords: Açaí berry; aging; band 3 protein function; d-Galactose; erythrocytes; glycation; oxidative stress; plasma membrane.

Figures

PLoS One. 2014 Mar 3;9(3):e89933. doi: 10.1371/journal.pone.0089933. eCollection 2014.

Açaí (Euterpe oleracea Mart.) modulates oxidative stress resistance in Caenorhabditis elegans by direct and indirect mechanisms

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PMID: 24594796 PMCID: PMC3940722 DOI: 10.1371/journal.pone.0089933

Free PMC article

Abstract

Açaí (Euterpe oleracea Mart.) has recently emerged as a promising source of natural antioxidants. Despite its claimed pharmacological and nutraceutical value, studies regarding the effects of açaí in vivo are limited. In this study, we use the Caenorhabditis elegans model to evaluate the in vivo antioxidant properties of açaí on an organismal level and to examine its mechanism of action. Supplementation with açaí aqueous extract (AAE) increased both oxidative and osmotic stress resistance independently of any effect on reproduction and development. AAE suppressed bacterial growth, but this antimicrobial property did not influence stress resistance. AAE-increased stress resistance was correlated with reduced ROS production, the prevention of sulfhydryl (SH) level reduction and gcs-1 activation under oxidative stress conditions. Our mechanistic studies indicated that AAE promotes oxidative stress resistance by acting through DAF-16 and the osmotic stress response pathway OSR-1/UNC-43/SEK-1. Finally, AAE increased polyglutamine protein aggregation and decreased proteasome activity. Our findings suggest that natural compounds available in AAE can improve the antioxidant status of a whole organism under certain conditions by direct and indirect mechanisms.

Figures

Randomized Controlled Trial Clin Nutr. 2020 May;39(5):1464-1469.
doi: 10.1016/j.clnu.2019.06.008. Epub 2019 Jun 12.

Effects of a hypoenergetic diet associated with açaí (Euterpe oleracea Mart.) pulp consumption on antioxidant status, oxidative stress and inflammatory biomarkers in overweight, dyslipidemic individuals

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PMID: 31307842 DOI: 10.1016/j.clnu.2019.06.008

Abstract

Objective: To evaluate the effects of a hypoenergetic diet (HD)associated with açaí pulp consumption on oxidative stress, antioxidant status and inflammatory biomarkers in overweight, dyslipidemic individuals.

Research methods & procedures: A randomized, double-blind, placebo-controlled clinical trial was conducted for 90 days. The study began with a 30-day run-in period, during which the intervention was exclusively a HD. Following this period, volunteers were randomized into 2 groups, and 200 g of either açaí pulp or placebo were added to the HD for 60 days. Anthropometric measurements, arterial pressure, oxidative stress and antioxidant status biomarkers, inflammatory and biochemical biomarkers were evaluated.

Results: Sixty-nine volunteers completed the clinical trial, 30 of which were in the HD + açaí group and 39 in HD + placebo group. Plasma 8-isoprostane concentrations significantly reduced 60 days after the intervention in the açaí group ($p = 0.000$), and there was a significant difference between the groups (açaí versus placebo; $p = 0.037$). Regarding inflammatory status parameters, a significant reduction in IL-6 was observed in the HD + açaí group ($p = 0.042$), and IFN-γ decreased significantly in both groups, HD + açaí ($p = 0.001$) and HD + placebo ($p = 0.008$); there were, however, no differences between the groups. Lipid profile parameters and blood glucose levels did not show change, regardless of nutritional intervention.

Conclusion: The addition of açaí to a HD, for 60 days, reduced oxidative stress and improved inflammation in overweight, dyslipidemic individuals.

Keywords: Acai Berry; Dyslipidemia; Euterpe; Inflammation; Obesity; Oxidative stress.

Int J Food Sci Nutr. 2021 Aug;72(5):650-652. doi: 10.1080/09637486.2020.1852192.
Epub 2020 Nov 30.

Blueberry benefits to cognitive function across the lifespan

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PMID: 33249925 DOI: 10.1080/09637486.2020.1852192

Abstract

It is well known that what we eat can influence our physical wellbeing, but interest is also increasing in the relationship between our diet and cognitive health. In recent years, blueberries have risen from relative obscurity to superfood status following a number of published epidemiological studies, rodent trials, and human RCTs, that suggest blueberries may convey benefits to cognition and mood. This commentary explores some of the evidence in humans, particularly during periods of cognitive development in the young and cognitive decline in the elderly. Evidence for possible mechanisms of action are also described. There is little doubt that blueberries convey a small, but tangible, benefit to cognitive function. Effects are seen following dose sizes easily achievable within a normal diet. Nevertheless, further research is needed on the cognitive domains influenced, additional benefits of longer-term supplementation, mechanisms of action responsible, and the real-world relevance of the cognitive benefits attained.

Keywords: Blueberries; ageing; anthocyanins; cognition; development; mood.

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Full Text Sources

Taylor & Francis

Review Curr Drug Metab. 2016;17(4):345-58. doi: 10.2174/1389200216666151103115654.

Coenzyme Q10 Supplementation and Exercise in Healthy Humans: A Systematic Review

Alvaro Sarmiento, Javier Diaz-Castro, Mario Pulido-Moran, Naroa Kajarabille, Rafael Guisado, Julio J Ochoa [1]

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PMID: 26526835 DOI: 10.2174/1389200216666151103115654

Abstract

Objective: Coenzyme Q10 (CoQ10) is an endogenous lipid-soluble benzoquinone compound that functions as a diffusible electron carrier in the electron transport chain. It is prevalent in all human tissues and organs, although it is mainly biosynthesised and concentrated in tissues with high energy turnover. The aim of this review was to perform an exhaustive analysis of the influence and effects of CoQ10 supplementation on parameters related to exercise in healthy humans, and to clarify the current state of knowledge of this field of study, presenting the relevant data in a systematic manner.

Method: This paper describes a transversal descriptive systematic review of published research in this field; the study was conducted using a method adapted from the PRISMA guidelines. The inclusion criteria applied were based on the PICO (population, intervention, comparison, and outcome) model.

Results: The database search performed yielded 372 citations. Finally, 13 studies met all the inclusion criteria and were incorporated in the present review.

Conclusion: CoQ10 has properties related to bioenergetic and antioxidant activity; thus, it is intimately involved in energy production and in the prevention of peroxidative damage to membrane phospholipids and of free radical-induced oxidation. These properties make it suitable as a dietary supplement to improve cellular bioenergetics and to inhibit certain age-related pathologies.

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources

Bentham Science Publishers Ltd.
Ingenta plc

Clinical Trial Free Radic Res. 2002 Apr;36(4):445-53. doi: 10.1080/10715760290021306.

Cellular redox activity of coenzyme Q10: effect of CoQ10 supplementation on human skeletal muscle

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Affiliations

PMID: 12069109 DOI: 10.1080/10715760290021306

Abstract

In this paper, we report results obtained from a continuing clinical trial on the effect of coenzyme Q10 (CoQ10) administration on human vastus lateralis (quadriceps) skeletal muscle. Muscle samples, obtained from aged individuals receiving placebo or CoQ10 supplementation (300mg per day for four weeks prior to hip replacement surgery) were analysed for changes in gene and protein expression and in muscle fibre type composition. Microarray analysis (Affymetrix U95A human oligonucleotide array) using a change in gene expression of 1.8-fold or greater as a cutoff point, demonstrated that a total of 115 genes were differentially expressed in six subject comparisons. In the CoQ10-treated subjects, 47 genes were up-regulated and 68 down-regulated in comparison with placebo-treated subjects. Restriction fragment differential display analysis showed that over 600 fragments were differentially expressed using a 2.0-fold or greater change in expression as a cutoff point. Proteome analysis revealed that, of the high abundance muscle proteins detected (2,086 +/- 115), the expression of 174 proteins was induced by CoQ10 while 77 proteins were repressed by CoQ10 supplementation. Muscle fibre types were also affected by CoQ10 treatment; CoQ10-treated individuals showed a lower proportion of type I (slow twitch) fibres and a higher proportion of type IIb (fast twitch) fibres, compared to age-matched placebo-treated subjects. The data suggests that CoQ10 treatment can act to influence the fibre type composition towards the fibre type profile generally found in younger individuals. Our results led us to the conclusion that coenzyme Q10 is a gene regulator and consequently has wide-ranging effects on over-all tissue metabolism. We develop a comprehensive hypothesis that CoQ10 plays a major role in the determination of membrane potential of many, if not all, sub-cellular membrane systems and that H2O2 arising from the activities of CoQ10 acts as a second messenger for the modulation of gene expression and cellular metabolism.

Related information

PubChem Compound (MeSH Keyword)

LinkOut - more resources

Meta-Analysis Complement Med Res. 2021;28(6):557-570. doi: 10.1159/000515249.
Epub 2021 Apr 16.

Diabetes, Age, and Duration of Supplementation Subgroup Analysis for the Effect of Coenzyme Q10 on Oxidative Stress: A Systematic Review and Meta-Analysis

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Affiliations
PMID: 33866314 DOI: 10.1159/000515249

Abstract in English, German

Background: Coenzyme Q10 (CoQ10) has been known as ubiquinone or ubidecarenone, which is a kind of lipid-soluble and vitamin-like antioxidant. It has a potent antioxidant effect against oxidation status via various mechanisms, including its ability to regenerate other antioxidants, such as vitamin E and vitamin C, and to increase antioxidant enzymes. Moreover, CoQ10 can quench free radicals and prevent lipid peroxidation. The aim of this systematic review and meta-analysis was to evaluate the effect of CoQ10 on oxidative stress variables.

Methods: A comprehensive electronic database search in Scopus, Web of Science, Embase, Cochrane Library, and Medline was performed to identify eligible randomized clinical trials. A meta-analysis of included studies was performed on selected variables using a random-effects model. Quality assessment was conducted by means of the Cochrane risk of bias assessment tool.

Results: To evaluate the effect of CoQ10 supplementation, 17 trials and 972 participants were included for the meta-analysis. The pooled analysis of primary studies showed that CoQ10 increased serum total antioxidant capacity (standardized mean difference [SMD] 0.62 mmol/L, 95% CI 0.18-1.05, I2 = 76.1%, $p < 0.001$) and superoxide dismutase (SMD 0.40 U/mg, 95% CI 0.12-0.67, I2 = 9.6%, $p < 0.345$) levels and decreased malondialdehyde (SMD -1.02 mmol/L, 95% CI -1.60 to -0.44, I2 = 88.2%, $p < 0.001$) level significantly compared to the placebo group. Although the effect of CoQ10 on nitric oxide (SMD 1.01 µmol/L, 95% CI -1.53 to 3.54, $p < 0.001$, I2 = 97.8%) and glutathione peroxidase (SMD -0.01 mmol/L, 95% CI -0.86 to 0.84, $p < 0.001$, I2 = 88.6%) was not significant, CoQ10 can be mentioned as an improvement in antioxidant defense status against reactive oxygen species.

Conclusion: These supplements have positive effects on antioxidant defense against oxidizing agents and elevate antioxidant enzyme levels in the body. However, due to limited research the results should be taken with caution.

Meta-Analysis Eur J Clin Pharmacol. 2020 Nov;76(11):1483-1499.
doi: 10.1007/s00228-020-02919-8. Epub 2020 Jun 25.

Coenzyme Q10 supplementation and oxidative stress parameters: a systematic review and meta-analysis of clinical trials

Abolfazl Akbari [1], Gholam Reza Mobini [2], Shahram Agah [1], Mojgan Morvaridzadeh [3], Amirhossein Omidi [3], Eric Potter [4], Siavash Fazelian [5], Seyed Hossein Ardehali [6], Elnaz Daneshzad [7], Sadegh Dehghani [8]

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PMID: 32583356 DOI: 10.1007/s00228-020-02919-8

Abstract

Purpose: Oxidative stress (OS) is associated with several chronic complications and diseases. The use of coenzyme Q10 (CoQ10) as an adjuvant treatment with routine clinical therapy against metabolic diseases has shown to be beneficial. However, the impact of CoQ10 as a preventive agent against OS has not been systematically investigated.

Methods: A systematic literature search was performed using the PubMed, SCOPUS, EMBASE, and Cochrane Library databases to identify randomized clinical trials evaluating the efficacy of CoQ10 supplementation on OS parameters. Standard mean differences and 95% confidence intervals were calculated for net changes in OS parameters using a random-effects model.

Results: Seventeen randomized clinical trials met the eligibility criteria to be included in the meta-analysis. Overall, CoQ10 supplementation was associated with a statistically significant decrease in malondialdehyde (MDA) (SMD - 0.94; 95% CI - 1.46, - 0.41; I^2 = 87.7%) and a significant increase in total antioxidant capacity (TAC) (SMD 0.67; 95% CI 0.28, 1.07; I^2 = 74.9%) and superoxide dismutase (SOD) activity (SMD 0.40; 95% CI 1.12, 0.67; I^2 = 9.6%). The meta-analysis found no statistically significant impact of CoQ10 supplementation on nitric oxide (NO) (SMD - 1.40; 95% CI - 0.12, 1.93; I^2 = 92.6%), glutathione (GSH) levels (SMD 0.41; 95% CI - 0.09, 0.91; I^2 = 70.0%), catalase (CAT) activity (SMD 0.36; 95% CI - 0.46, 1.18; I^2 = 90.0%), or glutathione peroxidase (GPx) activities (SMD - 1.40; 95% CI: - 0.12, 1.93; I^2 = 92.6%).

Conclusion: CoQ10 supplementation, in the tested range of doses, was shown to reduce MDA concentrations, and increase TAC and antioxidant defense system enzymes. However, there were no significant effects of CoQ10 on NO, GSH concentrations, or CAT activity.

Keywords: Coenzyme Q10; Glutathione peroxidase; Malondialdehyde; Oxidative stress.

Related information

Review Int J Dermatol. 2021 Dec;60(12):1449-1461. doi: 10.1111/ijd.15518.
Epub 2021 Mar 20.

Effects of hydrolyzed collagen supplementation on skin aging: a systematic review and meta-analysis

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Affiliations
PMID: 33742704 DOI: 10.1111/ijd.15518

Abstract

Skin aging has become a recurring concern even for younger people, mainly owing to increased life expectancy. In this context, the use of nutricosmetics as supplements has increased in recent years. Moreover, numerous scientific studies have shown the benefits of hydrolyzed collagen supplementation in improving the signs of skin aging. The objective of this study was to summarize the evidence on the effects of hydrolyzed collagen supplementation on human skin through a systematic review followed by a meta-analysis of clinical trials focusing on the process of skin aging. A literature search was conducted in the Medline, Embase, Cochrane, LILACS (Latin American and Caribbean Health Sciences Literature), and Journal of Negative Results in BioMedicine databases. Eligible studies were randomized, double-blind, and controlled trials that evaluated oral supplementation with hydrolyzed collagen as an intervention and reported at least one of the following outcomes: skin wrinkles, hydration, elasticity, and firmness. After retrieving articles from the databases, 19 studies were selected, with a total of 1,125 participants aged between 20 and 70 years (95% women). In the meta-analysis, a grouped analysis of studies showed favorable results of hydrolyzed collagen supplementation compared with placebo in terms of skin hydration, elasticity, and wrinkles. The findings of improved hydration and elasticity were also confirmed in the subgroup meta-analysis. Based on results, ingestion of hydrolyzed collagen for 90 days is effective in reducing skin aging, as it reduces wrinkles and improves skin elasticity and hydration.

Keywords: clinical trials; collagen.

Related information

MedGen

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Full Text Sources

Randomized Controlled Trial Eur J Nutr. 2015 Mar;54(2):251-63.
doi: 10.1007/s00394-014-0706-z. Epub 2014 May 5.

Randomized controlled trial of oral glutathione supplementation on body stores of glutathione

John P Richie Jr [1], Sailendra Nichenametla, Wanda Neidig, Ana Calcagnotto, Jeremy S Haley, Todd D Schell, Joshua E Muscat

Affiliations
PMID: 24791752 DOI: 10.1007/s00394-014-0706-z

Abstract

Purpose: Glutathione (GSH), the most abundant endogenous antioxidant, is a critical regulator of oxidative stress and immune function. While oral GSH has been shown to be bioavailable in laboratory animal models, its efficacy in humans has not been established. Our objective was to determine the long-term effectiveness of oral GSH supplementation on body stores of GSH in healthy adults.

Methods: A 6-month randomized, double-blinded, placebo-controlled trial of oral GSH (250 or 1,000 mg/day) on GSH levels in blood, erythrocytes, plasma, lymphocytes and exfoliated buccal mucosal cells was conducted in 54 non-smoking adults. Secondary outcomes on a subset of subjects included a battery of immune markers.

Results: GSH levels in blood increased after 1, 3 and 6 months versus baseline at both doses. At 6 months, mean GSH levels increased 30-35 % in erythrocytes, plasma and lymphocytes and 260 % in buccal cells in the high-dose group ($P < 0.05$). GSH levels increased 17 and 29 % in blood and erythrocytes, respectively, in the low-dose group ($P < 0.05$). In most cases, the increases were dose and time dependent, and levels returned to baseline after a 1-month washout period. A reduction in oxidative stress in both GSH dose groups was indicated by decreases in the oxidized to reduced glutathione ratio in whole blood after 6 months. Natural killer cytotoxicity increased >twofold in the high-dose group versus placebo ($P < 0.05$) at 3 months.

Conclusions: These findings show, for the first time, that daily consumption of GSH supplements was effective at increasing body compartment stores of GSH.

Trial registration: ClinicalTrials.gov NCT01044277.

Comment in

Commentary to "Randomized controlled trial of oral glutathione supplementation on body stores of glutathione".
Guilford FT.

Randomized Controlled Trial Planta Med. 2020 Jul;86(11):749-759.
doi: 10.1055/a-1170-7785. Epub 2020 May 19.

Phenolic-rich Pomegranate Peel Extract: In Vitro, Cellular, and In Vivo Activities for Skin Hyperpigmentation Treatment

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PMID: 32428937 DOI: 10.1055/a-1170-7785

Abstract

The pomegranate phenolics are reported to have cutaneous benefits and to be effective in treating skin disorders, including hyperpigmentation. In this context, a preparation method was developed by which to obtain phenolic-rich pomegranate peel extract. Sinapic acid was presented as the major pomegranate peel phenolics, followed by gallic and ellagic acids, and 4 additional phenolics. The extract exhibited strong antioxidant activity with an *in vitro* tyrosinase inhibitory effect. The skin hyperpigmentation treating potency was confirmed by the suppression of cellular melanogenesis through tyrosinase and TRP-2 inhibitions as examined in the B16F10 melanoma cells. Cellular antioxidant and proliferative activities of the extract toward human dermal fibroblasts were evidenced, as well as an inhibitory effect against MMP-2. The extract was developed into the stable serum and mask. The products were proved to be non-irritated in 30 Thai volunteers participating in a single application closed patch test. A split-face, randomized, double-blind, placebo-controlled test of the skin lightening effect was evaluated in the 30 volunteers over 28 consecutive daily treatments and monitored by the Mexameter MX 18. The active serum and mask were better in facial skin lightening efficacy than the placebo ($p < 0.005$). That was in accordance with the sensory evaluation scored by the volunteers. Phenolic-rich pomegranate peel extract is evidenced as a safe herbal derived material promising for skin hyperpigmentation treatment. Supportive information regarding chemical and biological profiles is presented with the confirmed safety and cutaneous benefits in volunteers.

Related information

MedGen

LinkOut - more resources

Meta-Analysis Crit Rev Food Sci Nutr. 2019;59(10):1605-1618.
doi: 10.1080/10408398.2017.1422480. Epub 2018 Jan 23.

Effect of resveratrol on blood pressure: A systematic review and meta-analysis of randomized, controlled, clinical trials

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Affiliations
PMID: 29359958 DOI: 10.1080/10408398.2017.1422480

Abstract

Introduction: Results of previous clinical trials evaluating the effect of resveratrol supplementation on blood pressure (BP) are controversial. ***Purpose:*** We aimed to assess the impact of resveratrol on BP through systematic review of literature and meta-analysis of available randomized, controlled clinical trials (RCTs). ***Methods:*** Literature search included SCOPUS, PubMed-Medline, ISI Web of Science and Google Scholar databases up to 17th October 2017 to identify RCTs investigating the impact of resveratrol on BP. Two review authors independently extracted data on study characteristics, methods and outcomes. Overall, the impact of resveratrol on BP was reported in 17 trials. ***Results:*** Administration of resveratrol did not significantly affect neither systolic BP [weighted mean difference (WMD): -2.5 95% CI:(-5.5, 0.6) mmHg; p=0.116; I^2=62.1%], nor diastolic BP [WMD: -0.5 95% CI:(-2.2, 1.3) mmHg; p=0.613; I^2=50.8], nor mean BP [*MAP*; WMD: -1.3 95% CI:(-2.8, 0.1) mmHg; p=0.070; I^2=39.5%] nor pulse pressure [*PP*; WMD: -0.9 95% CI:(-3.1, 1.4) mmHg; p=0.449; I^2=19.2%]. However, significant WMDs were detected in subsets of studies categorized according to high resveratrol daily dosage (≥300 mg/day) and presence of diabetes. Meta-regression analysis revealed a positive association between systolic BP-lowering resveratrol activity (slope: 1.99; 95% CI: 0.05, 3.93; two-tailed p= 0.04) and Body Mass Index (BMI) at baseline, while no association was detected neither between baseline BMI and MAP-lowering resveratrol activity (slope: 1.35; 95% CI: -0.22, 2.91; two-tailed p= 0.09) nor between baseline BMI and PP-lowering resveratrol activity (slope: 1.03; 95% CI: -1.33, 3.39; two-tailed p= 0.39). Resveratrol was fairly well-tolerated and no serious adverse events occurred among most of the eligible trials. ***Conclusion:*** The favourable effect of resveratrol emerging from the current meta-analysis suggests the possible use of this nutraceutical as active compound in order to promote cardiovascular health, mostly when used in high daily dose (≥300 mg/day) and in diabetic patients.

Keywords: Resveratrol; blood pressure; meta-analysis; metaregression; type 2 diabetes.

Related information

Meta-Analysis Phytother Res. 2021 Dec;35(12):6754-6767. doi: 10.1002/ptr.7262.
Epub 2021 Sep 2.

Effect of resveratrol on C-reactive protein: An updated meta-analysis of randomized controlled trials

Armita Mahdavi Gorabi [1], Saeed Aslani [2], Danyal Imani [3], Bahman Razi [4], Thozhukat Sathyapalan [5], Amirhossein Sahebkar [6 7 8 9]

Affiliations
PMID: 34472150 DOI: 10.1002/ptr.7262

Abstract

We conducted a meta-analysis on the available randomized clinical trials (RCTs) to assess the role of resveratrol in lowering C-reactive protein (CRP) and high-sensitivity CRP (hs-CRP) levels, as markers of inflammation, in various inflammatory disorders. Literature search through Medline/PubMed, Scopus, ISI Web of Science, and Cochrane Library yielded 35 RCTs (24 studies for hs-CRP and 11 studies for CRP). Pooled results revealed that resveratrol supplementation significantly reduced the hs-CRP (MWD = -0.40 mg/L; 95% CI: -0.70 to -0.09 mg/L; p = .01) and CRP (MWD = -0.31 mg/L; 95% CI: -0.47 to -0.15 mg/L; p < .001) levels in serum. Subgroup analysis revealed that resveratrol in group with ≥10 weeks significantly reduces hs-CRP levels (MWD = -0.48 mg/L; 95% CI: -0.92 to -0.04 mg/L; p = .03) and CRP (WMD = -0.47 mg/L, 95% CI = -0.69 to -0.25, p < .001). A dose of ≥500 mg/day supplementation improves the levels of CRP, but not hs-CRP. This meta-analysis demonstrates that resveratrol consumption is effective in lowering the levels of CRP and hs-CRP in inflammatory conditions, especially if supplementation takes place for ≥10 weeks with ≥500 mg/day.

Keywords: CRP; hs-CRP; inflammation; meta-analysis; randomized clinical trial; resveratrol.

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources
Ovid Technologies, Inc.
Wiley

Review Phytother Res. 2022 Sep;36(9):3529-3539. doi: 10.1002/ptr.7562.
Epub 2022 Jul 14.

Resveratrol supplementation efficiently improves endothelial health: A systematic review and meta-analysis of randomized controlled trials

Nazanin Mohammadipoor [1], Fatemeh Shafiee [1], Amirabbas Rostami [2], Mohammad Saeed Kahrizi [3], Hamidreza Soleimanpour [4], Majid Ghodsi [5], Mohammad Javed Ansari [6], Dmitry Olegovich Bokov [7] [8], Behrooz Jannat [9], Erfan Mosharkesh [10], Mohammad Sadegh Pour Abbasi [11]

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PMID: 35833325 DOI: 10.1002/ptr.7562

Abstract

We perform a systematic review and meta-analysis of randomized controlled trials (RCTs) to quantify the effect of resveratrol supplementation on endothelial function. A comprehensive search was performed in electronic databases including PubMed, Scopus, Web of Science, and Cochrane Library up to February 2021 with no limitation in time and language. A meta-analysis of eligible studies was performed using a random-effects model to estimate the pooled effect size of flow-mediated dilation (FMD), intracellular adhesion molecule-1 (ICAM-1), vascular adhesion molecule-1 (VCAM-1), fibrinogen, and plasminogen activator inhibitor-1 (PAI-1). In total, 21 arms from 17 studies were included. The meta-analysis results showed that resveratrol significantly change the concentrations of FMD (WMD: 1.43%; 95% CI: 0.98 to 1.88, $p < .001$) and ICAM-1 (WMD: -7.09 ng/ml, 95% CI: -7.45 to -6.73, $p < .001$). However, VCAM-1, fibrinogen, and PAI-1 did not change significantly after resveratrol supplementation. In conclusion, the results of this study suggest that resveratrol supplementation can improve endothelial function which could be important, especially in patients with cardiovascular diseases.

Keywords: endothelial function; meta-analysis; resveratrol; systematic review.

Related information

PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources
Ovid Technologies, Inc.

Meta-Analysis Obes Rev. 2019 Mar;20(3):487-498. doi: 10.1111/obr.12775.
Epub 2018 Dec 5.

Resveratrol supplementation significantly influences obesity measures: a systematic review and dose-response meta-analysis of randomized controlled trials

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PMID: 30515938 DOI: 10.1111/obr.12775

Abstract

This study aimed to summarize earlier randomized controlled trials on the effects of resveratrol supplementation on body weight (BW), body mass index (BMI), waist circumference (WC) and fat mass (FM). We searched PubMed, SCOPUS, Cochrane Library and Google Scholar from inception to April 2018 using relevant keywords. All clinical trials investigating the effects of resveratrol supplementation on BW, BMI, WC and FM in adults were included. Overall, 28 trials were included. Pooled effect sizes suggested a significant effect of resveratrol administration on weight (weighted mean differences [WMD]: -0.51 kg, 95% confidence interval [CI]: -0.94 to -0.09; I^2 = 50.3%, P = 0.02), BMI (WMD: -0.17 kg m^{-2} , 95% CI: -0.32, -0.03; I^2 = 49.6%, P = 0.02) and WC (WMD: -0.79 cm, 95% CI: -1.39, -0.2; I^2 = 13.4%, P = 0.009), respectively. However, no significant effect of resveratrol supplementation on FM was found (WMD: -0.36%, 95% CI: -0.88, 0.15; I^2 = 0.0%, P = 0.16). Findings from subgroup analysis revealed a significant reduction in BW and BMI in trials using resveratrol at the dosage of <500 mg d^{-1} , those with long-term interventions (≥3 month), and performed on people with obesity. Taken together, the data suggest that resveratrol supplementation has beneficial effects to reduce BW, BMI and WC, but not FM.

Keywords: dose-response; meta-analysis; obesity; resveratrol; weight.

Related information

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PubChem Compound (MeSH Keyword)

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Review Biofactors. 2018 Jan;44(1):69-82. doi: 10.1002/biof.1400. Epub 2017 Dec 6.

Effect of resveratrol and pterostilbene on aging and longevity

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PMID: 29210129 DOI: 10.1002/biof.1400

Abstract

Over the past years, several studies have found that foods rich in polyphenols protect against age-related disease, such as atherosclerosis, cardiovascular disease, cancer, arthritis, cataracts, osteoporosis, type 2 diabetes (T2D), hypertension and Alzheimer's disease. Resveratrol and pterostilbene, the polyphenol found in grape and blueberries, have beneficial effects as anti-aging compounds through modulating the hallmarks of aging, including oxidative damage, inflammation, telomere attrition and cell senescence. In this review, we discuss the relationship between resveratrol and pterostilbene and possible aging biomarker, including oxidative stress, inflammation, and high-calorie diets. Moreover, we also discuss the positive effect of resveratrol and pterostilbene on lifespan, aged-related disease, and health maintenance. Furthermore, we summarize a variety of important mechanisms modulated by resveratrol and pterostilbene possibly involved in attenuating age-associated disorders. Overall, we describe resveratrol and pterostilbene potential for prevention or treatment of several age-related diseases by modulating age-related mechanisms. © 2017 BioFactors, 44(1):69-82, 2018.

Keywords: aging; healthspan; lifespan; pterostilbene; resveratrol.

Related information

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PubChem Compound (MeSH Keyword)

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Medical

Nanomedicine (Lond). 2020 Dec;15(28):2801-2817. doi: 10.2217/nnm-2020-0289.
Epub 2020 Nov 16.

Resveratrol: nanocarrier-based delivery systems to enhance its therapeutic potential

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PMID: 33191840 DOI: 10.2217/nnm-2020-0289

Abstract

Resveratrol (3,5,4'-trihydroxystilbene) is a polyphenolic compound existing in trees, peanuts and grapes and exhibits a broad spectrum of promising therapeutic activities, but it is unclear whether this entity targets the sites of action after oral administration. *In vivo* applicability of resveratrol has limited success so far, mainly due to its incompetent systemic delivery resulting from its low water solubility, poor bioavailability and short biological half-life. First-pass metabolism and presence of enterohepatic recirculation create doubt on the biological application of high doses typically used for *in vitro* trials. To augment bioavailability, absorption and uptake of resveratrol by cellular internalization, countless approaches have been implemented which involve the use of nanocarriers. Nanocarriers are a well-known delivery system used to reduce first-pass hepatic metabolism, overcome enterohepatic recirculation and accelerate the absorption of drugs *via* lymphatic pathways.

Keywords: dendrimers; enterohepatic recirculation; immunomodulator; liposomes; nanofibers; nanoparticles; niosomes; resveratrol; self-emulsifying systems; transferosomes.

Related information

PubChem Compound (MeSH Keyword)

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Meta-Analysis Food Funct. 2018 Dec 13;9(12):6116-6128. doi: 10.1039/c8fo01259h.

The effects of resveratrol supplementation on biomarkers of inflammation and oxidative stress among patients with metabolic syndrome and related disorders: a systematic review and meta-analysis of randomized controlled trials

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PMID: 30426122 DOI: 10.1039/c8fo01259h

Abstract

There are several current trials investigating the effect of resveratrol supplementation on biomarkers of inflammation and oxidative stress among patients with metabolic syndrome (MetS); however, their findings are controversial. This systematic review and meta-analysis of randomized controlled trials (RCTs) were conducted to summarize the existing evidence and collectively determine the effects of resveratrol supplementation on biomarkers of inflammation and oxidative stress among patients with MetS and related disorders. Two authors independently searched electronic databases, including MEDLINE, EMBASE, Cochrane Library, and Web of Science databases, until May 2018 in order to find relevant RCTs. The quality of the selected RCTs was evaluated using the Cochrane Collaboration risk of bias tool. Cochran's Q test and I-square (I2) statistic were used to determine whether heterogeneity exists across included trials. Standardized mean difference (SMD) and 95% CI between two intervention groups were used to determine pooled effect sizes. Out of 317 potential citations selected based on keywords, 24 RCTs met the inclusion criteria and were eligible for the current meta-analysis. The pooled results obtained by using the random-effects model showed that resveratrol supplementation significantly decreased C-reactive protein (CRP) (SMD = -0.55; 95% CI, -0.84, -0.26; P < 0.001; I2: 84.0) and tumor necrosis factor-α (TNF-α) (SMD = -0.68; 95% CI, -1.08, -0.28; P = 0.001; I2: 81.3) concentrations among patients with MetS and related disorders. Interleukin 6 (IL-6) (SMD = 0.05; 95% CI, -0.31, 0.41; P = 0.79; I2: 85.0) and superoxide dismutase (SOD) (SMD = 0.21; 95% CI, -3.16, 3.59; P = 0.90; I2: 97.7) concentrations did not significantly change following resveratrol supplementation. Resveratrol supplementation showed a promising lowering effect on some of the inflammatory markers among patients with MetS and related disorders. Additional prospective studies regarding the effect of resveratrol supplementation on biomarkers of inflammation and oxidative stress by using higher doses of resveratrol and longer duration of supplementation are necessary.

Meta-Analysis Am J Clin Nutr. 2014 Jun;99(6):1510-9. doi: 10.3945/ajcn.113.082024.
Epub 2014 Apr 2.

Effect of resveratrol on glucose control and insulin sensitivity: a meta-analysis of 11 randomized controlled trials

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PMID: 24695890 DOI: 10.3945/ajcn.113.082024
Free article

Abstract

Background: The results of human clinical trials investigating the effects of resveratrol on glucose control and insulin sensitivity are inconsistent.

Objective: We aimed to quantitatively evaluate the effects of resveratrol on glucose control and insulin sensitivity.

Design: We performed a strategic literature search of PubMed, Embase, MEDLINE, and the Cochrane Library (updated to March 2014) for randomized controlled trials that estimated the effects of resveratrol on glucose control and insulin sensitivity. Study quality was assessed by using the Jadad scale. Weighted mean differences were calculated for net changes in glycemic measures by using fixed-effects or random-effects models. We performed prespecified subgroup and sensitivity analyses to evaluate potential heterogeneity. Meta-regression analyses were conducted to investigate dose effects of resveratrol on fasting glucose and insulin concentrations in nondiabetic subjects.

Results: Eleven studies comprising a total of 388 subjects were included in this meta-analysis. Resveratrol consumption significantly reduced fasting glucose, insulin, glycated hemoglobin, and insulin resistance (measured by using the homeostatic model assessment) levels in participants with diabetes. No significant effect of resveratrol on glycemic measures of nondiabetic participants was found in the meta-analysis. Subgroup and sensitivity analyses indicated that the pooled effects of resveratrol on fasting glucose and insulin concentrations in nondiabetic participants were not affected by body mass index, study design, resveratrol dose, study duration, or Jadad score.

Conclusions: Resveratrol significantly improves glucose control and insulin sensitivity in persons with diabetes but does not affect glycemic measures in nondiabetic persons. Additional high-quality studies are needed to further evaluate the potential benefits of resveratrol in humans.

Meta-Analysis Clin Ther. 2018 Jul;40(7):1180-1192.e5. doi: 10.1016/j.clinthera.2018.05.015.
Epub 2018 Jul 23.

Effect of Resveratrol Supplementation on Inflammatory Markers: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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PMID: 30017172 DOI: 10.1016/j.clinthera.2018.05.015

Abstract

Purpose: The evidence has suggested that resveratrol has anti-inflammatory effect; however, the results are inconsistent and inconclusive. The aim of this study was to assess the effect of resveratrol supplementation on the levels of inflammatory markers through a systematic review and meta-analysis of available randomized controlled trials (RCTs).

Methods: A search strategy was completed using Medline, ISI Web of Science, Directory of Open Access Journal, SID, ProQuest, Cochrane Library, Scopus, and EMBASE up to May 2017, to identify placebo-controlled RCTs that assessed resveratrol effects on circulating (serum and plasma) inflammatory markers (interleukin [IL]-6, tumor necrosis factor-α [TNF-α], and high-sensitivity C-reactive protein [hs-CRP]) among adult participants aged 17 years and older in 17 RCTs with a total of 736 subjects. The evaluation of study quality was performed using the Jadad scale. Weighted mean difference (WMD) was calculated for evaluating the changes in the inflammatory markers using fixed-effects or random-effects models. We performed subgroup and sensitivity analyses to evaluate the heterogeneity of the studies.

Findings: Seventeen RCTs, including 736 subjects, fulfilled the eligibility criteria and were selected for analyses. The results of meta-analysis found significant reductions in the level of TNF-α (WMD, -0.44; 95% CI, -0.71 to -0.164; P = 0.002; Q statistic = 21.60; I^2 = 49.1%; P = 0.02) and hs-CRP (WMD, -0.27; 95% CI, -0.5 to -0.02; P = 0.033; Q statistic = 26.95; I^2 = 51.8%; P = 0.013) after supplementation with resveratrol. Resveratrol supplementation had no significant effect on the level of IL-6 (WMD, -0.16; 95% CI, -0.53 to 0.20; P = 0.38; Q statistic = 36.0; I^2 = 72.3%; P = 0.001). Statistically significant heterogeneity was observed for the type of sample in IL-6 and study duration in inflammatory markers IL-6, TNF-α, and hs-CRP.

Implications: Available evidence from RCTs suggests that resveratrol supplementation significantly reduced TNF-α and hs-CRP levels. Significant improvement in inflammatory markers support resveratrol as an adjunct to pharmacologic management of metabolic diseases.

Keywords: TNF-α; hs-CRP; inflammation; meta-analysis; resveratrol; systematic review.

Review Eur J Nutr. 2021 Sep;60(6):2961-2977. doi: 10.1007/s00394-021-02623-y.
Epub 2021 Jul 12.

Can resveratrol modulate sirtuins in obesity and related diseases? A systematic review of randomized controlled trials

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PMID: 34251517 DOI: 10.1007/s00394-021-02623-y

Abstract

Purpose: Human sirtuins can be a powerful therapeutic target in preventing and treating obesity and age-related diseases. Some dietary components can modulate sirtuins' activity, such as resveratrol. This systematic review aimed to assess whether resveratrol (RSV), without other interventions, can stimulate sirtuins in the treatment of excess weight and its comorbidities.

Methods: MEDLINE/Pubmed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were used for search eligible articles. Randomized clinical trials assessing RSV supplementation on changes in the sirtuins' gene expression/protein levels was the primary outcome. Other possible changes in cardiometabolic markers were considered the second outcome. Following PRISMA guidelines and using predefined inclusion and exclusion criteria, two reviewers independently and in parallel screened, assessed the studies' quality, and compiled data. Disagreements were resolved by consensus or consulting a third author.

Results: This review included seven randomized control trials. Four articles demonstrated a significant increase in SIRT-1 with different RSV dosages and interventions time. The secondary outcomes showed improvements in insulin sensitivity, lipid profile, metabolic flexibility, total antioxidant capacity, energy expenditure changes, and reduction of ectopic accumulation of fat.

Conclusion: Data from RCTs studies showed that RSV supplementation could stimulate SIRT-1 in humans, and therefore contribute to the treatment of excess weight and its comorbidities. However, more research is needed because it was not possible to confirm this effect truly. [PROSPERO registration number: CRD42020205571].

Keywords: Noncommunicable diseases; Obesity; Overweight; Resveratrol; SIRT-1; Sirtuins.

Related information

Review Int J Mol Sci. 2022 Apr 5;23(7):4027. doi: 10.3390/ijms23074027.

Benefits and Implications of Resveratrol Supplementation on Microbiota Modulations: A Systematic Review of the Literature

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Affiliations

PMID: 35409389 PMCID: PMC8999966 DOI: 10.3390/ijms23074027

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Abstract

Resveratrol is a polyphenol that has been shown to possess many applications in different fields of medicine. This systematic review has drawn attention to the axis between resveratrol and human microbiota, which plays a key role in maintaining an adequate immune response that can lead to different diseases when compromised. Resveratrol can also be an asset in new technologies, such as gene therapy. PubMed, Cochrane Library, Scopus, Web of Science, and Google Scholar were searched to find papers that matched our topic dating from 1 January 2017 up to 18 January 2022, with English-language restriction using the following Boolean keywords: ("resveratrol" AND "microbio*"). Eighteen studies were included as relevant papers matching the purpose of our investigation. Immune response, prevention of thrombotic complications, microbiota, gene therapy, and bone regeneration were retrieved as the main topics. The analyzed studies mostly involved resveratrol supplementation and its effects on human microbiota by trials in vitro, in vivo, and ex vivo. The beneficial activity of resveratrol is evident by analyzing the changes in the host's genetic expression and the gastrointestinal microbial community with its administration. The possibility of identifying individual microbial families may allow to tailor therapeutic plans with targeted polyphenolic diets when associated with microbial dysbiosis, such as inflammatory diseases of the gastrointestinal tract, degenerative diseases, tumors, obesity, diabetes, bone tissue regeneration, and metabolic syndrome.

Int J Pharm. 2021 Oct 25;608:121086. doi: 10.1016/j.ijpharm.2021.121086. Epub 2021 Sep 14.

Efficacy of a resveratrol nanoformulation based on a commercially available liposomal platform

Carla Caddeo [1], Daniela Lucchesi [2], Xavier Fernàndez-Busquets [3], Donatella Valenti [4], Giuseppe Penno [2], Anna Maria Fadda [4], Laura Pucci [5]

Affiliations

PMID: 34530099 DOI: 10.1016/j.ijpharm.2021.121086

Abstract

Scalability is one of the important factors slowing down or even impeding the clinical translation of nanoparticle-based systems. The latter need to be manufactured at a high level of quality, with batch-to-batch reproducibility, and need to be stable after the manufacturing process, during long-term storage and upon clinical administration. In this study, a vesicular formulation intended for cutaneous applications was developed by the easy reconstitution of a commercially available liposomal platform. Resveratrol, a naturally occurring compound with potent antioxidant activity, and Tween80, a hydrophilic non-ionic surfactant, were included in the formulation. The physico-chemical properties of the vesicles were assessed using light scattering and cryogenic transmission electron microscopy. Nanosized (around 80 nm) spherical and elongated, unilamellar vesicles were produced, with remarkable storage stability. The incorporation of resveratrol in the vesicular system did not alter its strong antioxidant activity, as demonstrated by antioxidant colorimetric assays (DPPH and FRAP). Furthermore, the resveratrol liposomes were cytocompatible with fibroblasts and capable of protecting skin cells from oxidative stress by reducing both endogenous and chemically induced reactive oxygen species more effectively than free resveratrol. Therefore, the proposed formulation, based on the use of a commercially available liposomal platform, represents an easy-to-prepare, reproducible, up-scaled and efficient means of delivering resveratrol and potentiating its biological activity in vitro.

Keywords: Antioxidant; Commercial liposomes; Resveratrol; Skin cells; Skin delivery.

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