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Efficacy of vitamin E in the conservative treatment of Peyronie's disease: legend or reality? A controlled study of 70 cases

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SUMMARY
The medical treatment is indicated in the development stage of Peyronie's disease (PD) for at least 1 year after diagnosis and whenever in case of penile pain. This research was conducted to demonstrate the possible effectiveness of vitamin E in PD treatment, whereas in the scientific literature this topic is much discussed. A total of 70 patients (age:26–69 years, mean: 54.1 ± 9.71) diagnosed with PD were enrolled in a conservative treatment. In addition to medical histories and physical examinations all patients underwent the following tests: International Index of Erectile Function (IIEF) questionnaire, penile ultrasound and photographic documentation, pain evaluation by a conventional 10-point pain scale Visual analogue pain scale (VAS). All 70 patients were divided into two different treatment groups: A and B, with different combinations of drugs: A = vitamin E + verapamil (injection + iontophoresis) + blueberries + propolis + topical diclofenac; B = verapamil (injection + iontophoresis) + blueberries + propolis + topical diclofenac.
All patients were treated for 6 months after which they underwent the same follow-up tests as performed prior to the treatment. Intergroup analysis revealed statistically significant differences: in the vitamin E group the effective plaque size reduction was _50.2% whereas in the control group the reduction was _35.8% (p = 0.027). In group A the improvement of curvature occurred in 96.6% of the cases whereas in the control group B this occurred in 48.4% (p = 0.0001), moreover, the mean curvature decrease was respectively _12.25° and _6.73° (p = 0.01). IIEF score was significantly improved in group A patients with comorbidities and erectile dysfunction (p = 0.025). Increase in plaque size occurred only in the control group (17.1%) (p = 0.032). We can affirm that vitamin E can help to prevent the progression of PD. This study strongly supports the recommendation that the best approach for treating PD is multimodal therapy.

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Protective Effects of Haematococcus Astaxanthin on Oxidative Stress in Healthy Smokers

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Abstract

Free radicals induced by cigarette smoking have been strongly linked to increased oxidative stress in vivo, contributing to the pathobiology of various diseases. This study was performed to investigate the effects of Haematococcus astaxanthin (ASX), which has been known to be a potent antioxidant, on oxidative stress in smokers. Thirty-nine heavy smokers (‡ 20 cigarettes/day) and 39 non-smokers were enrolled in this study. Smokers were randomly divided into three dosage groups to receive ASX at doses of 5, 20, or 40 mg (n = 13, each) once daily for 3 weeks. Oxidative stress biomarkers such as malondialdehyde, isoprostane, supe-

roxide dismutase, and total antioxidant capacity, and ASX levels in plasma were measured at baseline and after 1, 2, and 3 weeks of treatment. Compared with baseline, the plasma malondialdehyde and isoprostane levels decreased, whereas superoxide dismutase level and total antioxidant capacity increased in all ASX intervention groups over the 3-week period. In particular, isoprostane levels showed a significant dose-dependent decrease after ASX intake. The results suggest that ASX supplementation might prevent oxidative damage in smokers by suppressing lipid peroxidation and stimulating the activity of the antioxidant system in smokers.

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Astaxanthin inhibits inflammation and fibrosis in the liver and adipose tissue of mouse models of diet-induced obesity and nonalcoholic steatohepatitis

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Abstract

The objective of this study was to determine if astaxanthin (ASTX), a xanthophyll carotenoid, can prevent obesity-associated metabolic abnormalities, inflammation and fibrosis in diet-induced obesity (DIO) and nonalcoholic steatohepatitis (NASH) mouse models. Male C57BL/6J mice were fed a low-fat (6% fat, w/w), a high-fat/high-sucrose control (HF/HS; 35% fat, 35% sucrose, w/w), or a HF/HS containing ASTX (AHF/HS; 0.03% ASTX, w/w) for 30 weeks. To induce NASH, another set of mice was fed a HF/HS diet containing 2% cholesterol (HF/HS/HC) a HF/HS/HC with 0.015% ASTX (AHF/HS/HC) for 18 weeks. Compared to LF, HF/HS significantly increased plasma total cholesterol, triglyceride and glucose, which were lowered by ASTX. ASTX decreased hepatic mRNA levels of markers of macrophagesand fibrosis in both models. The effect of ASTX was more prominent in NASH than DIO mice. In epididymal fat, ASTX also decreased macrophage infiltration and M1 macrophage marker expression, and inhibited hypoxia-inducible factor 1-α and its downstream fibrogenic genes in both mouse models. ASTX significantly decreased tumor necrosis factor α mRNA in the splenocytes from DIO mice upon lipopolysaccharides stimulation compared with those from control mice fed an HF/HS diet. Additionally, ASTX significantly elevated the levels of genes that regulate fatty acid β-oxidationand mitochondrial biogenesis in the skeletal muscle compared with control obese mice, whereas no differences were noted in adipose lipogenic genes. Our results indicate that ASTX inhibits inflammation and fibrosis in the liver and adipose tissue and enhances the skeletal muscle's capacity for mitochondrial fatty acid oxidation in obese mice.

Clinical Trial

BJU In. 2001 Jul;88(1):63-7. doi: 10.1046/j.1464-410x.2001.02241.x.

Acetyl-L-carnitine vs tamoxifen in the oral therapy of Peyronie's disease: a preliminary report

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Abstract

Objective: To detect whether oral acetyl-L-carnitine might be useful in the acute and early chronic phases of Peyronie's disease, compared with tamoxifen, a drug currently in use.

Patients and methods: The study included 48 patients with Peyronie's disease (15 acute and 33 initial chronic), randomized equally into two groups. The first group used tamoxifen 20 mg twice daily for 3 months and the second acetyl-L-carnitine 1 g twice daily for 3 months. The disease and stages were diagnosed and identified using a history, objective examination, pharmacologically induced erection, autophotography during erection, and basic and dynamic colour Doppler ultrasonography. Penile curvature, plaque size, pain and disease progression were assessed. The differences between the groups or between the variables before and after therapy were compared using analysis of variance or the chi-squared test.

Results: Acetyl-L-carnitine was significantly more effective than tamoxifen in reducing pain and in inhibiting disease progression. Acetyl-L-carnitine reduced penile curvature significantly, while tamoxifen did not; both drugs significantly reduced plaque size. Tamoxifen induced significantly more side-effects than acetyl-L-carnitine.

Conclusions: These results suggest that acetyl-L-carnitine is significantly more effective and safe than tamoxifen in the therapy of acute and early chronic Peyronie's disease.

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Randomized Controlled Trial

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Safety and efficacy of coenzyme Q10 supplementation in early chronic Peyronie's disease: a double-blind, placebo-controlled randomized study

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Abstract

No oral medication has proved to be clearly beneficial for Peyronie's disease (PD). We investigated the safety and efficacy of coenzyme Q(10) (CoQ(10)) supplementation in patients with early chronic PD. We conducted a randomized clinical trial of 186 patients with chronic early PD. Patients were randomly assigned to either 300 mg CoQ(10) daily (n=93) or similar regimen of placebo (n=93) for 24 weeks. Erectile function (EF), pain during erection, plaque volume, penile curvature and treatment satisfaction using patient versions of the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) questionnaire were assessed at baseline and every 4 weeks during study period. EF was assessed using International Index of Erectile Function (IIEF-5), and pain was evaluated with a visual analog scale (VAS, 0-10). All patients also responded to a Global Assessment Question, 'Has the treatment you have been taking during this study improved your erections?' After 24 weeks, mean IIEF-5 score, mean VAS score and mean EDITS score improved significantly in patients receiving CoQ(10) (all P<0.01). Mean plaque size and mean penile curvature degree were decreased in the CoQ(10) group, whereas a slight increase was noted in the placebo group (both P=0.001). Mean index of IIEF-5 in 24-week treatment period was 17.8 ± 2.7 in the CoQ(10) group and 8.8 ± 1.5 in the placebo group (P=0.001). Of the patients in CoQ(10) group, 11 (13.6%) had disease progression vs 46 (56.1%) in placebo group (P=0.01). In patients with early chronic PD, CoQ(10) therapy leads plaque size and penile curvature reduction and improves EF.

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L-arginine and phosphodiesterase (PDE) inhibitors counteract fibrosis in the Peyronie's fibrotic plaque and related fibroblast cultures

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Abstract

Inducible nitric oxide synthase (iNOS) is expressed in both the fibrotic plaque of Peyronie's disease (PD) in the human, and in the PD-like plaque elicited by injection of TGFbeta1 into the penile tunica albuginea (TA) of the rat. Long-term inhibition of iNOS activity, presumably by blocking nitric oxide (NO)- and cGMP-mediated effects triggered by iNOS expression, exacerbates tissue fibrosis through an increase in: (a) collagen synthesis, (b) levels of reactive oxygen species (ROS), and (c) the differentiation of fibroblasts into myofibroblasts. We have now investigated whether: (a) phosphodiesterase (PDE) isoforms,

that regulate the interplay of cGMP and cAMP pathways, are expressed in both the human and rat TA; and (b) L-arginine, that stimulates NOS activity and hence NO synthesis, and PDE inhibitors, that increase the levels of cGMP and/or cAMP, can inhibit collagen synthesis and induce fibroblast/myofibroblast apoptosis, thus acting as antifibrotic agents. We have found by immunohistochemistry, RT/PCR, and Western blot that PDE5A-3 and PDE4A, B, and D variants are indeed expressed in human and rat normal TA and PD plaque tissue, as well as in their respective fibroblast cultures. As expected, in the PD fibroblast cultures, pentoxifylline (non-specific cAMP-PDE inhibitor) increased cAMP levels without affecting cGMP levels, whereas sildenafil (PDE5A inhibitor) raised cGMP levels. Both agents and L-arginine reduced the expression of collagen I (but not collagen III) and the myofibroblast marker, alpha-smooth muscle actin, as determined by immunocytochemistry and quantitative image analysis. These effects were mimicked by incubation with 8-Br-cGMP, which in addition increased apoptosis, as measured by TUNEL. When L-arginine (2.25 g/kg/day), pentoxifylline (10 mg/kg/day), or sildenafil (10 mg/kg/day) was given individually in the drinking water for 45 days to rats with a PD-like plaque induced by TGF beta1, each treatment resulted in a 80-95% reduction in both plaque size and in the collagen/fibroblast ratio, as determined by Masson trichrome staining. Both sildenafil and pentoxiphylline stimulated fibroblast apoptosis within the TA. Our results support the hypothesis that the increase in NO and/or cGMP/cAMP levels by long-term administration of nitrergic agents or inhibitors of PDE, may be effective in reversing the fibrosis of PD, and more speculatively, other fibrotic conditions.

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Review

Overview of *Salvia miltiorrhiza* as a Potential Therapeutic Agent for Various Diseases: An Update on Efficacy and Mechanisms of Action

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Abstract: *Salvia miltiorrhiza* Bunge (*S. miltiorrhiza*) is a medicinal herb that has been used for the treatment for various diseases such as cardiovascular and cerebrovascular diseases in East Asia including Korea. Considering its extensive usage as a therapeutic agent for multiple diseases, there is a need to review previous research regarding its therapeutic benefits and their mechanisms. Therefore, we searched PubMed and PubMed Central for articles reporting its therapeutic effects on certain disease groups including cancers, cardiovascular, liver, and nervous system diseases. This review provides an overview of therapeutic benefits and targets of *S. miltiorrhiza*, including inflammation, fibrosis, oxidative stress, and apoptosis. The findings on multi-functional properties of *S. miltiorrhiza* discussed in this article support the efficacy of *S. miltiorrhiza* extract on various diseases, but also call for further research on the multiple mechanisms that mediate its therapeutic effects.