Testro-X Research Review

A compilation of research demonstrating the effectiveness of each ingredient in Testro-X.

Testro-X contains:

- Magnesium
- Zinc
- KSM-66 Ashwagandha
- Forskolin
- Inositol
- Glycine
- L-Theanine
- Boron
- Black Pepper Fruit Extract

Magnesium:

Biol Trace Elem Res. 2011 Apr;140(1):18-23. doi: 10.1007/s12011-010-8676-3. Epub 2010 Mar 30.

Effects of magnesium supplementation on testosterone levels of athletes and sedentary subjects at rest and after exhaustion.

Cinar V[1], Polat Y, Baltaci AK, Mogulkoc R.

Author information

Abstract

This study was performed to assess how 4 weeks of magnesium supplementation and exercise affect the free and total plasma testosterone levels of sportsmen practicing tae kwon do and sedentary controls at rest and after exhaustion. The testosterone levels were determined at four different periods: resting before supplementation, exhaustion before supplementation, resting after supplementation, and exhaustion after supplementation in three study groups, which are as follows: Group 1-sedentary controls supplemented with 10 mg magnesium per kilogram body weight. Group 2-tae kwon do athletes practicing 90-120 min/day supplemented with 10 mg magnesium per kilogram body weight. Group 3-tae kwon do athletes practicing 90-120 min/day receiving no magnesium supplements. The free plasma testosterone levels increased at exhaustion before and after supplementation compared to resting levels. Exercise also increased testosterone levels relative to sedentary subjects. Similar increases were observed for total testosterone. Our results show that supplementation with magnesium increases free and total testosterone values in sedentary and in athletes. The increases are higher in those who exercise than in sedentary individuals.

PMID: 20352370 DOI: 10.1007/s12011-010-8676-3

[PubMed - indexed for MEDLINE]

Key Takeaway:

Magnesium supplementation was found to increase both free and total testosterone counts in both sedentary and active men.

Int J Androl. 2011 Dec;34(6 Pt 2):e594-600. doi: 10.1111/j.1365-2605.2011.01193.x. Epub 2011 Jun 15.

Magnesium and anabolic hormones in older men.

Maggio M[1], Ceda GP, Lauretani F, Cattabiani C, Avantaggiato E, Morganti S, Ablondi F, Bandinelli S, Dominguez LJ, Barbagallo M, Paolisso G, Semba RD, Ferrucci L.

Author information

Abstract

Optimal nutritional and hormonal statuses are determinants of successful ageing. The age associated decline in anabolic hormones such as testosterone and insulin-like growth factor 1 (IGF-1) is a strong predictor of metabolic syndrome, diabetes and mortality in older men. Studies have shown that magnesium intake affects the secretion of total IGF-1 and increase testosterone bioactivity. This observation suggests that magnesium can be a modulator of the anabolic/catabolic equilibrium disrupted in the elderly people. However, the relationship between magnesium and anabolic hormones in men has not been investigated. We evaluated 399 ≥65-year-old men of CHIANTI in a study population representative of two municipalities of Tuscany (Italy) with complete data on testosterone, total IGF-1, sex hormone binding globulin (SHBG), dehydroepiandrosterone sulphate (DHEAS) and serum magnesium levels. Linear regression models were used to test the relationship between magnesium and testosterone and IGF-1. Mean age of the population was 74.18 ± 6.43 (years ± SD, age range 65.2-92.4). After adjusting for age, magnesium was positively associated with total testosterone (β ± SE, 34.9 ± 10.3; p = 0.001) and with total IGF-1 (β ± SE, 15.9 ± 4.8; p = 0.001). After further adjustment for body mass index (BMI), log (IL-6), log (DHEAS), log (SHBG), log (insulin), total IGF-1, grip strength, Parkinson's disease and chronic heart failure, the relationship between magnesium and total testosterone remained strong and highly significant (β ± SE, 48.72 ± 12.61; p = 0.001). In the multivariate analysis adjusted for age, BMI, log (IL-6), liver function, energy intake, log (insulin), log (DHEAS), selenium, magnesium levels were also still significantly associated with IGF-1 (β ± SE, 16.43 ± 4.90; p = 0.001) and remained significant after adjusting for total testosterone (β ± SE, 14.4 ± 4.9; p = 0.01). In a cohort of older men, magnesium levels are strongly and independently associated with the anabolic hormones testosterone and IGF-1.

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PMID: 21675994 PMCID: PMC4623306 DOI: 10.1111/j.1365-2605.2011.01193.x

[PubMed - indexed for MEDLINE] **Free PMC Article**

Key Takeaway:

Magnesium supplementation is linked to higher testosterone production in older males. “Magnesium levels are strongly and independently associated with the anabolic hormones testosterone and IGF-1.”

Int J Endocrinol. 2014;2014:525249. doi: 10.1155/2014/525249. Epub 2014 Mar 3.

The Interplay between Magnesium and Testosterone in Modulating Physical Function in Men.

Maggio M[1], De Vita F[2], Lauretani F[2], Nouvenne A[3], Meschi T[1], Ticinesi A[2], Dominguez LJ[4], Barbagallo M[4], Dall'aglio E[1], Ceda GP[1].

Author information

Abstract

The role of nutritional status as key factor of successful aging is very well recognized. Among the different mechanisms by which nutrients may exert their beneficial effects is the modulation of the hormonal anabolic milieu, which is significantly reduced with aging. Undernutrition and anabolic hormonal deficiency frequently coexist in older individuals determining an increased risk of mobility impairment and other adverse outcomes. Mineral assessment has received attention as an important determinant of physical performance. In particular, there is evidence that magnesium exerts a positive influence on anabolic hormonal status, including Testosterone, in men. In this review we summarize data from observational and intervention studies about the role of magnesium in Testosterone bioactivity and the potential underlying mechanisms of this relationship in male subjects. If larger studies will confirm these pivotal data, the combination of hormonal and mineral replacements might be adopted to prevent or delay the onset of disability in the elderly.

PMID: 24723948 PMCID: PMC3958794 DOI: 10.1155/2014/525249

[PubMed] **Free PMC Article**

Key Takeaway:

There is strong evidence that magnesium exerts a positive influence on anabolic hormonal status, particularly with testosterone, in men.

Zinc:

Neuro Endocrinol Lett. 2006 Feb-Apr;27(1-2):247-52.

The effect of exhaustion exercise on thyroid hormones and testosterone levels of elite athletes receiving oral zinc.

Kilic M[1], Baltaci AK, Gunay M, Gökbel H, Okudan N, Cicioglu I.

Author information

Abstract

OBJECTIVES: The present study aims to investigate how exhaustion exercise affects thyroid hormones and testosterone levels in elite athletes who are supplemented with oral zinc sulfate for 4 weeks.

METHODS: The study included 10 male wrestlers, who had been licensed wrestlers for at least 6 years. Mean age of the wrestlers who volunteered in the study was 18.70 +/- 2.4 years. All subjects were supplemented with oral zinc sulfate (3 mg/kg/day) for 4 weeks in addition to their normal diet. Thyroid hormone and testosterone levels of all subjects were determined as resting and exhaustion before and after zinc supplementation.

RESULTS: Resting TT3, TT4, FT3, FT4 and TSH levels of subjects were higher than the parameters measured after exhaustion exercise before zinc supplementation ($p<0.05$). Both resting and exhaustion TT3, TT4 and FT3 values after 4-week zinc supplementation were found significantly higher than both of the parameters (resting and exhaustion) measured before zinc supplementation ($p<0.05$). Resting total testosterone and free testosterone levels before zinc supplementation were significantly higher than exhaustion levels before zinc supplementation ($p<0.05$). Both resting and exhaustion total and free testosterone levels following 4-week zinc supplementation were found significantly higher than the levels (both resting and exhaustion) measured before zinc supplementation ($p<0.05$).

CONCLUSION: Findings of our study demonstrate that exhaustion exercise led to a significant inhibition of both thyroid hormones and testosterone concentrations, but that 4-week zinc supplementation prevented this inhibition in wrestlers. In conclusion, physiological doses of zinc administration may benefit performance.

PMID: 16648789

[PubMed - indexed for MEDLINE]

Key Takeaway:

Zinc supplementation leads to higher production of thyroid hormones and testosterone in exercising men.

Neuro Endocrinol Lett. 2007 Oct;28(5):681-5.

Effect of fatiguing bicycle exercise on thyroid hormone and testosterone levels in sedentary males supplemented with oral zinc.

Kilic M[1].

Author information

Abstract

OBJECTIVE: The aim of this study was to determine how exercise affects thyroid hormones and testosterone levels in sedentary men receiving oral zinc for 4 weeks.

METHODS: The study included 10 volunteers (mean age, 19.47+/-1.7 years) who did not exercise. All subjects received supplements of oral zinc sulfate (3 mg/kg/day) for 4 weeks and their normal diets. The thyroid hormone and testosterone levels of all subjects were determined at rest and after bicycle exercise before and after zinc supplementation.

RESULTS: TT3, TT4, FT3, and total and free testosterone levels decreased after exercise compared to resting levels before supplementation ($p<0.01$). Both the resting and fatigue hormone values were higher after 4 weeks of supplementation than the resting and fatigue values before supplementation ($p<0.05$).

CONCLUSION: The results indicate that exercise decreases thyroid hormones and testosterone in sedentary men; however, zinc supplementation prevents this decrease. Administration of a physiologic dose of zinc can be beneficial to performance.

PMID: 17984944

[PubMed - indexed for MEDLINE]

Key Takeaway:

Zinc supplementation leads to higher free testosterone, total testosterone, T3 and T4 thyroid hormones in sedentary men.

Ren Fail. 2010 May;32(4):417-9. doi: 10.3109/08860221003706958.

Impact of oral zinc therapy on the level of sex hormones in male patients on hemodialysis.

Jalali GR[1], Roozbeh J, Mohammadzadeh A, Sharifian M, Sagheb MM, Hamidian Jahromi A, Shabani S, Ghaffarpasand F, Afshariani R.

Author information

Abstract

BACKGROUND: Sexual dysfunction in chronic renal failure patients undergoing hemodialysis is common. It is demonstrated that the zinc level is significantly lower in the hemodialysis patients.

OBJECTIVE: In this clinical trial, we investigate the effect of zinc supplement therapy on the serum levels of sexual hormones in hemodialysis male patients.

PATIENTS AND METHODS: We carried out a clinical trial study including 100 of our male patients with end-stage renal disease on hemodialysis. Testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and zinc plasma level were measured in all of the patients. The patients received zinc supplement (zinc sulfate, 250 mg/day) for 6 weeks, and sex hormones and zinc plasma level were checked again.

RESULTS: Serum level of FSH and prolactin did not have any significant changes before and after intervention, but serum level of testosterone, LH, and zinc increased significantly.

DISCUSSION: These results suggest that although zinc administration did not have a definite effect on hemodialysis patients with sexual dysfunction, it can cause increase in the serum level of sex hormones which may improve the sexual function of the patients in some aspects.

PMID: 20446777 DOI: 10.3109/08860221003706958

[PubMed - indexed for MEDLINE]

Key Takeaway:

Correcting a zinc deficiency leads to a rapid increase in testosterone production.

Arch Androl. 1981 Aug;7(1):69-73.

Effect of zinc administration on plasma testosterone, dihydrotestosterone, and sperm count.

Netter A, Hartoma R, Nahoul K.

Abstract

The effects of zinc therapy on plasma testosterone (T), dihydrotestosterone (DHT), and sperm count were studied in 37 patients with idiopathic infertility of more than five years duration. In the first group (T less than 4.8 ng/ml; 22 patients), T and DHT rose significantly after oral administration of zinc, as did the sperm count. Nine wives became pregnant, six within 3 months and three within 2 months of a second trial. In the second group (T greater than or equal to 4.8 ng/ml; 15 patients), T and sperm count were unaffected by zinc, while DHT increased significantly. There was no conception observed. The rationale of this treatment and the significance of the results are discussed.

PMID: 7271365

[PubMed - indexed for MEDLINE]

Key Takeaway:

Correcting a zinc deficiency leads to more balanced T, DHT, and increased sperm count.

Neuro Endocrinol Lett. 2006 Feb-Apr;27(1-2):267-70.

Zinc supplementation in rats subjected to acute swimming exercise: Its effect on testosterone levels and relation with lactate.

Kaya O[1], Gokdemir K, Kilic M, Baltaci AK.

Author information

Abstract

OBJECTIVE: There is fairly scarce information about the effects of zinc, an essential trace element, on performance. Studies concerned with the relation between zinc and exercise mostly concentrate on the distribution of this element in the body in response to exercise. The objective of the present study is to explore how zinc supplementation affects testosterone levels and its relation with lactate in rats subjected to acute swimming exercise.

MATERIALS AND METHODS: Thirty adult male rats of Sprague-Dawley species were equally allocated to 3 groups. Group 1: Control. Group 2: Group subjected to 30-minute acute swimming exercise. Group 3: Group supplemented with intraperitoneal (i.p.) zinc (3 mg/kg day) for 4 weeks and subjected to 30-minute swimming exercise. Blood samples collected from all experimental animals by decapitation method were analyzed to determine free and total testosterone and lactate levels in the plasma.

RESULTS: Group 3 had the highest free and total testosterone levels, followed by Group 1 and Group 2. The highest lactate levels were found in Group 2 and the levels in Group 3 were higher than those in Group 1.

CONCLUSION: Results of the study demonstrate that zinc supplementation leads to a significant increase in testosterone levels and a significant decrease in lactate levels. In conclusion, physiological doses of zinc supplementation can be useful for performance.

PMID: 16648790

[PubMed - indexed for MEDLINE]

Key Takeaway:

Zinc supplementation has been found to elevate LH production, Testosterone, and thyroid functioning.

J Nutr. 1996 Apr;126(4):842-8.

Dietary zinc deficiency alters 5 alpha-reduction and aromatization of testosterone and androgen and estrogen receptors in rat liver.

Om AS[1], Chung KW.

Author information

Abstract

We studied the effects of zinc deficiency on hepatic androgen metabolism and aromatization, androgen and estrogen receptor binding, and circulating levels of reproductive hormones in freely fed, pair-fed and zinc deficient rats. Hepatic conversion of testosterone to dihydrotestosterone was significantly less, but formation of estradiol from testosterone was significantly greater in rats fed the zinc-deficient diet compared with freely fed and pair-fed control rats. There were significantly lower serum concentrations of luteinizing hormone, estradiol and testosterone in rats fed the zinc-deficient diet. No difference in the concentration of serum follicle-stimulating hormone was observed between the zinc-deficient group and either control group. Scatchard analyses of the receptor binding data showed a significantly higher level of estrogen receptor in zinc-deficient rats (36.6 +/- 3.4 fmol/mg protein) than in pair-fed controls (23.3 +/- 2.2 fmol/mg protein) and a significantly lower level of androgen binding sites in rats fed the zinc-deficient diet (6.7 +/- 0.7 fmol/mg protein) than in pair-fed control rats (11.3 +/- 1.2 fmol/mg protein). There were no differences in hepatic androgen and estrogen receptor levels between freely fed and pair-fed controls. These findings indicate that zinc deficiency reduces circulating luteinizing hormone and testosterone concentrations, alters hepatic steroid metabolism, and modifies sex steroid hormone receptor levels, thereby contributing to the pathogenesis of male reproductive dysfunction.

PMID: 8613886

[PubMed - indexed for MEDLINE]

Key Takeaway:

Zinc deficiency leads to a 59% reduction in androgen receptors.

Ashwagandha:

J Int Soc Sports Nutr. 2015 Nov 25;12:43. doi: 10.1186/s12970-015-0104-9. eCollection 2015.

Examining the effect of Withania somnifera supplementation on muscle strength and recovery: a randomized controlled trial.

Wankhede S[1], Langade D[2], Joshi K[3], Sinha SR[4], Bhattacharyya S[5].

Author information

Abstract

BACKGROUND: Withania somnifera (ashwagandha) is a prominent herb in Ayurveda. This study was conducted to examine the possible effects of ashwagandha root extract consumption on muscle mass and strength in healthy young men engaged in resistance training.

METHODS: In this 8-week, randomized, prospective, double-blind, placebo-controlled clinical study, 57 young male subjects (18-50 years old) with little experience in resistance training were randomized into treatment (29 subjects) and placebo (28 subjects) groups. Subjects in the treatment group consumed 300 mg of ashwagandha root extract twice daily, while the control group consumed starch placebos. Following baseline measurements, both groups of subjects underwent resistance training for 8 weeks and measurements were repeated at the end of week 8. The primary efficacy measure was muscle strength. The secondary efficacy measures were muscle size, body composition, serum testosterone levels and muscle recovery. Muscle strength was evaluated using the 1-RM load for the bench press and leg extension exercises. Muscle recovery was evaluated by using serum creatine kinase level as a marker of muscle injury from the effects of exercise.

RESULTS: Compared to the placebo subjects, the group treated with ashwagandha had significantly greater increases in muscle strength on the bench-press exercise (Placebo: 26.4 kg, 95% CI, 19.5, 33.3 vs. Ashwagandha: 46.0 kg, 95% CI 36.6, 55.5; p = 0.001) and the leg-extension exercise (Placebo: 9.8 kg, 95% CI, 7.2,12.3 vs. Ashwagandha: 14.5 kg, 95 % CI, 10.8,18.2; p = 0.04), and significantly greater muscle size increase at the arms (Placebo: 5.3 cm(2), 95% CI, 3.3,7.2 vs. Ashwagandha: 8.6 cm(2), 95% CI, 6.9,10.8; p = 0.01) and chest (Placebo: 1.4 cm, 95% CI, 0.8, 2.0 vs. Ashwagandha: 3.3 cm, 95% CI, 2.6, 4.1; p < 0.001). Compared to the placebo subjects, the subjects receiving ashwagandha also had significantly greater reduction of exercise-induced muscle damage as indicated by the stabilization of serum creatine kinase (Placebo: 1307.5 U/L, 95% CI, 1202.8, 1412.1, vs. Ashwagandha: 1462.6 U/L, 95% CI, 1366.2, 1559.1; p = 0.03), significantly greater increase in testosterone level (Placebo: 18.0 ng/dL, 95% CI, -15.8, 51.8 vs. Ashwagandha: 96.2 ng/dL, 95% CI, 54.7, 137.5; p = 0.004), and a significantly greater decrease in body fat percentage (Placebo: 1.5%, 95% CI, 0.4%, 2.6% vs. Ashwagandha: 3.5%, 95% CI, 2.0%, 4.9%; p = 0.03).

CONCLUSION: This study reports that ashwagandha supplementation is associated with significant increases in muscle mass and strength and suggests that ashwagandha supplementation may be useful in conjunction with a resistance training program.

Key Takeaway:

Ashwagandha supplementation raised the average subject's testosterone level from 630 ng/dL to 726 ng/dL and was associated with significant increases in muscle mass and strength.

Indian J Psychol Med. 2012 Jul;34(3):255-62. doi: 10.4103/0253-7176.106022.

A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults.

Chandrasekhar K[1], Kapoor J, Anishetty S.

Author information

Abstract

CONTEXT: Stress is a state of mental or emotional strain or tension, which can lead to underperformance and adverse clinical conditions. Adaptogens are herbs that help in combating stress. Ayurvedic classical texts, animal studies and clinical studies describe Ashwagandha as a safe and effective adaptogen.

AIMS: The aim of the study was to evaluate the safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha roots in reducing stress and anxiety and in improving the general well-being of adults who were under stress.

SETTINGS AND DESIGN: Single center, prospective, double-blind, randomized, placebo-controlled trial.

MATERIALS AND METHODS: A total of 64 subjects with a history of chronic stress were enrolled into the study after performing relevant clinical examinations and laboratory tests. These included a measurement of serum cortisol, and assessing their scores on standard stress-assessment questionnaires. They were randomized to either the placebo control group or the study drug treatment group, and were asked to take one capsule twice a day for a period of 60 days. In the study drug treatment group, each capsule contained 300 mg of high-concentration full-spectrum extract from the root of the Ashwagandha plant. During the treatment period (on Day 15, Day 30 and Day 45), a follow-up telephone call was made to all subjects to check for treatment compliance and to note any adverse reactions. Final safety and efficacy assessments were done on Day 60.

STATISTICAL ANALYSIS: t-test, Mann-Whitney test.

RESULTS: The treatment group that was given the high-concentration full-spectrum Ashwagandha root extract exhibited a significant reduction ($P<0.0001$) in scores on all the stress-assessment scales on Day 60, relative to the placebo group. The serum cortisol levels were substantially reduced ($P=0.0006$) in the Ashwagandha group, relative to the placebo group. The adverse effects were mild in nature and were comparable in both the groups. No serious adverse events were reported.

CONCLUSION: The findings of this study suggest that a high-concentration full-spectrum Ashwagandha root extract safely and effectively improves an individual's resistance towards stress and thereby improves self-assessed quality of life.

Key Takeaway:

300mg of KSM-66 ashwagandha was given to subjects for 60 days, reduced cortisol levels by 27%, along with greatly reducing anxiety and mental stress.

Evid Based Complement Alternat Med. 2009 Sep 29. [Epub ahead of print]

Withania somnifera Improves Semen Quality in Stress-Related Male Fertility.

Mahdi AA[1], Shukla KK, Ahmad MK, Rajender S, Shankhwar SN, Singh V, Dalela D.

Author information

Abstract

Stress has been reported to be a causative factor for male infertility. Withania somnifera has been documented in Ayurveda and Unani medicine system for its stress-combating properties. However, limited scientific literature is available on this aspect of W. somnifera. We undertook the present study to understand the role of stress in male infertility, and to test the ability of W. somnifera to combat stress and treat male infertility. We selected normozoospermic but infertile individuals (N = 60), further categorized in three groups: normozoospermic heavy smokers (N = 20), normozoospermics under psychological stress (N = 20) and normozoospermics with infertility of unknown etiology (N = 20). Normozoospermic fertile men (N = 60) were recruited as controls. The subjects were given root powder of W. somnifera at a rate of 5 g/day for 3 months. Measuring various biochemical and stress parameters before and after treatment, suggested a definite role of stress in male infertility and the ability of W. somnifera to treat stress-related infertility. Treatment resulted in a decrease in stress, improved the level of anti-oxidants and improved overall semen quality in a significant number of individuals. The treatment resulted in pregnancy in the partners of 14% of the patients.

PMID: 19789214 PMCID: PMC3136684 DOI: 10.1093/ecam/nep138

Key Takeaway: Cortisol reduction of 32% and significant improvement in fertility biomarkers.

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Withania somnifera Improves Semen Quality in Stress-Related Male Fertility

Abbas Ali Mahdi,[1] Kamla Kant Shukla,[1] Mohammad Kaleem Ahmad,[1] Singh Rajender,[2] Satya Narain Shankhwar,[3] Vishwajeet Singh,[3] and Deepansh Dalela[1]

[1]Department of Biochemistry, C.S.M. Medical University, Lucknow 26003, India
[2]Endrocrinology Division, Central Drug Research Institute, Lucknow 226001, India
[3]Department of Urology, C.S.M. Medical University, Lucknow 226003, India

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Abstract

Stress has been reported to be a causative factor for male infertility. *Withania somnifera* has been documented in Ayurveda and Unani medicine system for its stress-combating properties. However, limited scientific literature is available on this aspect of *W. somnifera*. We undertook the present study to understand the role of stress in male infertility, and to test the ability of *W. somnifera* to combat stress and treat male infertility. We selected normozoospermic but infertile individuals (N = 60), further categorized in three groups: normozoospermic heavy smokers (N = 20), normozoospermics under psychological stress (N = 20) and normozoospermics with infertility of unknown etiology (N = 20). Normozoospermic fertile men (N = 60) were recruited as controls. The subjects were given root powder of *W. somnifera* at a rate of 5 g/day for 3 months. Measuring various biochemical and stress parameters before and after treatment, suggested a definite role of stress in male infertility and the ability of *W. somnifera* to treat stress-related infertility. Treatment resulted in a decrease in stress, improved the level of anti-oxidants and improved overall semen quality in a significant number of individuals. The treatment resulted in pregnancy in the partners of 14% of the patients.

Fertil Steril. 2010 Aug;94(3):989-96. doi: 10.1016/j.fertnstert.2009.04.046. Epub 2009 Jun 6.

Withania somnifera improves semen quality by regulating reproductive hormone levels and oxidative stress in seminal plasma of infertile males.

Ahmad MK[1], Mahdi AA, Shukla KK, Islam N, Rajender S, Madhukar D, Shankhwar SN, Ahmad S.

Author information

Abstract

OBJECTIVE: To investigate the impact of Withania somnifera roots on semen profile, oxidative biomarkers, and reproductive hormone levels of infertile men.

DESIGN: Prospective study.

SETTING: Departments of Biochemistry and Urology, Chhatrapati Shahuji Maharaj Medical University, Lucknow, India.

PATIENT(S): Seventy-five normal healthy fertile men (control subjects) and 75 men undergoing infertility screening.

INTERVENTION(S): High-performance liquid chromatography assay procedure for quantization of vitamin A and E in seminal plasma. Biochemical parameters in seminal plasma were estimated by standard spectrophotometric procedures. Estimation of T, LH, FSH, and PRL in blood serum by RIA methods.

MAIN OUTCOME MEASURES(S): Before and after the treatment, seminal plasma biochemical parameters, antioxidant vitamins, and serum T, LH, FSH, and PRL levels were measured.

RESULT(S): Withania somnifera inhibited lipid peroxidation and protein carbonyl content and improved sperm count and motility. Treatment of infertile men recovered the seminal plasma levels of antioxidant enzymes and vitamins A, C, and E and corrected fructose. Moreover, treatment also significantly increased serum T and LH and reduced the levels of FSH and PRL.

CONCLUSION(S): The treatment with W. somnifera effectively reduced oxidative stress, as assessed by decreased levels of various oxidants and improved level of diverse antioxidants. Moreover, the levels of T, LH, FSH and PRL, good indicators of semen quality, were also reversed in infertile subjects after treatment with the herbal preparation.

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Key Takeaway: These two studies show massive increases in testosterone (40% and 16% in infertile subjects and 15% in healthy subjects) with significantly improved sperm quality, resulting in increased pregnancy rate in partners.

Evid Based Complement Alternat Med. 2013;2013:571420. doi: 10.1155/2013/571420. Epub 2013 Nov 28.

Clinical Evaluation of the Spermatogenic Activity of the Root Extract of Ashwagandha (Withania somnifera) in Oligospermic Males: A Pilot Study.

Ambiye VR[1], Langade D[2], Dongre S[3], Aptikar P[4], Kulkarni M[5], Dongre A[3].

Author information

Abstract

Ashwagandha (Withania somnifera) has been described in traditional Indian Ayurvedic medicine as an aphrodisiac that can be used to treat male sexual dysfunction and infertility. This pilot study was conducted to evaluate the spermatogenic activity of Ashwagandha root extract in oligospermic patients. Forty-six male patients with oligospermia (sperm count < 20 million/mL semen) were enrolled and randomized either to treatment (n = 21) with a full-spectrum root extract of Ashwagandha (675 mg/d in three doses for 90 days) or to placebo (n = 25) in the same protocol. Semen parameters and serum hormone levels were estimated at the end of 90-day treatment. There was a 167% increase in sperm count (9.59 ± 4.37 × 10(6)/mL to 25.61 ± 8.6 × 10(6)/mL; P < 0.0001), 53% increase in semen volume (1.74 ± 0.58 mL to 2.76 ± 0.60 mL; P < 0.0001), and 57% increase in sperm motility (18.62 ± 6.11% to 29.19 ± 6.31%; P < 0.0001) on day 90 from baseline. The improvement in these parameters was minimal in the placebo-treated group. Furthermore, a significantly greater improvement and regulation were observed in serum hormone levels with the Ashwagandha treatment as compared to the placebo. The present study adds to the evidence on the therapeutic value of Ashwagandha (Withania somnifera), as attributed in Ayurveda for the treatment of oligospermia leading to infertility.

PMID: 24371462 PMCID: PMC3863556 DOI: 10.1155/2013/571420

Key Takeaway:

Daily supplementation with KSM-66 ashwagandha for 90 days showed 17% increase in T production, 36% increase in LH production (T precursor), suggesting that ashwagandha stimulates testosterone production at the brain level in the pituitary gland.

Forskolin:

Pharmazie. 2012 Jan;67(1):5-13.

Forskolin and derivatives as tools for studying the role of cAMP.

Alasbahi RH[1], Melzig MF.

Author information

Abstract

Forskolin (7beta-acetoxy-1alpha,6beta,9alpha-trihydroxy-8,13-epoxy-labd-14-en-11-one) is the first main labdane diterpenoid isolated from the roots of the Indian Plectranthus barbatus ANDREWS and one of the most extensively studied constituents of this plant. The unique character of forskolin as a general direct, rapid and reversible activator of adenylyl cyclase not only underlies its wide range of pharmacological effects but also renders it as a valuable tool in the study of the role of cAMP. The purpose of this review is to provide data presenting the utility of forskolin--as a cAMP activator--for studying the function of cAMP from different biological viewpoints as follows: 1) Investigation on the role of cAMP in various cellular processes in different organs such as gastrointestinal tract, respiratory tract, reproductive organs, endocrine system, urinary system, olfactory system, nervous system, platelet aggregating system, skin, bones, eyes, and smooth muscles. 2) Studies on the role of cAMP activation and inhibition to understand the pathogenesis (e.g. thyroid autoimmune disorders, leukocyte signal transduction defect in depression, acute malaria infection, secretory dysfunction in inflammatory diseases) as well as its possibly beneficial role for curing diseases such as the regulation of coronary microvascular NO production after heart failure, the attenuation of the development or progression of fibrosis in the heart and lungs, the augmentation of myo-protective effects of ischemic preconditioning especially in the failing hearts after myocardial infarction, the stimulation of the regeneration of injured retinal ganglion cells, the curing of glaucoma and inflammatory diseases, the reducing of cyst formation early in the polycystic kidney disease, and the management of autoimmune disorders by enhancing Fas-mediated apoptosis. 3) Studies on the role of cAMP in the mechanism of actions of a number of drugs and substances such as the effect of the protoberberine alkaloid palmatine on the active ion transport across rat colonic epithelium, the inhibitory effect of retinoic acid on HIV-1-induced podocyte proliferation, the whitening activity of luteolin, the effect of cilostazol on nitric oxide production, an effect that is involved in capillary-like tube formation in human aortic endothelial cells, the apoptotic effect of bullatacin, the effects of paraoxon and chlorpyrifos oxon on nervous system. Moreover, cAMP was found to play a role in acute and chronic exposure to ethanol, in morphine dependence and withdrawal and in behavioral sensitization to cocaine as well as in the protection against cisplatin-induced oxidative injuries.

PMID: 22393824

Key Takeaway:

Forskolin is well-known for increasing levels of natural cAMP in humans.

Mol Cell Endocrinol. 1990 Mar 26;70(1):49-63.

Gonadotropin receptor occupancy and stimulation of cAMP and testosterone production by purified Leydig cells: critical dependence on cell concentration.

Browne ES[1], Flasch MV, Sohal GS, Bhalla VK.

Author information

Abstract

Rat testicular interstitial cells have been separated by discontinuous/continuous gradient of Percoll, yielding four cell fractions. The light cells in fraction I bound luteinizing hormone/human chorionic gonadotropin (LH/hCG) with high affinity but were not steroidogenic in response to hormone. Fraction II consisted mainly of germ cells. Although fraction III contained Leydig cells, this fraction was contaminated with germ cells and was less responsive to hormone as compared to the Leydig cells in fraction IV. The Leydig cells in fraction IV produced cAMP and testosterone in response to hormone action in a manner which was critically dependent upon cell concentration. The production of cyclic adenosine monophosphate (cAMP) in the presence of saturating concentrations of hCG (2.4 X 10(-10) M) was linear as a function of cell concentration up to 7.0 X 10(6) cells/1.25 ml and thereafter, a slight inhibition (26%) was seen at 10 X 10(6) cells/1.25 ml. The average value for cAMP production by hCG was 133.8 +/- 8.5 pmol cAMP/2 X 10(6) cells. The production of testosterone was biphasic, increasing linearly up to 5 X 10(6) cells/1.25 ml and decreasing thereafter. Two million cells, in the presence of 2.4 X 10(-10) M hCG, produced an average of 24.2 +/- 1.7 ng of testosterone in reaction volumes ranging from 1 to 2 ml whereas the same number of cells only produced 5.1 +/- 0.6 ng of testosterone in 250 microliters. The binding of 125I-labeled hCG to the same batch of cells increased with increasing cell concentrations as expected but under the conditions of maximal steroidogenesis at low cell concentrations (1.25, 2.0, and 2.5 X 10(6) cells/1.25 ml), it was barely detectable. Thus, we conclude that there is an inverse relationship between the parameters of binding and biological response in purified Leydig cells.

PMID: 2160383

Key Takeaway:

cAMP is well-known for its stimulatory effect on increasing natural testosterone production.

Activation of the Human Androgen Receptor through a Protein Kinase A Signaling Pathway*

Lynne V. Nazareth and **Nancy L. Weigel**‡

+ **Author Affiliations**

↵‡**To whom correspondence should be addressed: Dept. of Cell Biology, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030. Tel.: 713-798-6234; Fax: 713-790-1275.**

Abstract

Aberrant activation of the androgen receptor through signaling pathways independent of androgen may be responsible for the progression of prostate tumors to the rapidly proliferating androgen-independent state. In this study, the effects of protein kinase A modulators on human androgen receptor activity were tested. Using an adenoviral DNA delivery system, we demonstrate that the androgen receptor can be activated by a protein kinase A activator, forskolin, in the absence of androgen when androgen receptor is co-transfected into monkey kidney CV1 cells or human prostate PC-3 cells with androgen-responsive reporters. Immunoblotting reveals that there is no significant change in androgen receptor protein level following forskolin treatment, suggesting that the enhanced activity is due to activation of the receptor. This activation can be blocked by a protein kinase A inhibitor peptide. Two potent anti-androgens, casodex and flutamide, can significantly reduce this activation, confirming that the ligand-independent pathway is an androgen receptor-mediated phenomenon. An intact DNA binding domain of the receptor is critical for this alternate signaling pathway since mutants with reduced DNA binding ability are inactive. The phosphorylation status of the androgen receptor or associated proteins may critically modulate receptor activity and should be considered when designing improved approaches to prostate cancer therapy.

Key Takeaway:

cAMP also increases androgen receptor AR activation in humans.

J Cell Biochem. 2001 Jun 26-Jul 25;83(1):147-54.

Stimulatory effect of lactate on testosterone production by rat Leydig cells.

Lin H[1], Wang SW, Wang RY, Wang PS.

Author information

Abstract

Previously we found that the increased plasma testosterone levels in male rats during exercise partially resulted from a direct and luteinizing hormone (LH)-independent stimulatory effect of lactate on the secretion of testosterone. In the present study, the acute and direct effects of lactate on testosterone production by rat Leydig cells were investigated. Leydig cells from rats were purified by Percoll density gradient centrifugation subsequent to enzymatic isolation of testicular interstitial cells. Purified rat Leydig cells (1 x 10(5) cells/ml) were in vitro incubated with human chorionic gonadotropin (hCG, 0.05 IU/ml), forskolin (an adenylyl cyclase activator, 10(-5) M), or 8-bromo-adenosine-3':5'-cyclic monophosphate (8-Br-cAMP, 10(-4) M), SQ22536 (an adenylyl cyclase inhibitor, 10(-6)-10(-5) M), steroidogenic precursors (25-hydroxy-cholesterol, pregnenolone, progesterone, and androstenedione, 10(-5) M each), nifedipine (a L-type Ca(2+) channel blocker, 10(-5)-10(-4) M), or nimodipine (a potent L-type Ca(2+) channel antagonist, 10(-5)-10(-4) M) in the presence or absence of lactate at 34 degrees C for 1 h. The concentration of medium testosterone was measured by radioimmunoassay. Administration of lactate at 5-20 mM dose-dependently increased the basal testosterone production by 63-187% but did not alter forskolin- and 8-Br-cAMP-stimulated testosterone release in rat Leydig cells. Lactate at 10 mM enhanced the stimulation of testosterone production induced by 25-hydroxy-cholesterol in rat Leydig cells but not other steroidogenic precursors. Lactate (10 mM) affected neither 30- nor 60-min expressions of cytochrome P450 side chain cleavage enzyme (P450scc) and steroidogenic acute regulatory (StAR) protein. The lactate-stimulated testosterone production was decreased by administration of nifedipine or nimodipine. These results suggested that the physiological level of lactate stimulated testosterone production in rat Leydig cells through a mechanism involving the increased activities of adenylyl cyclase, cytochrome P450scc, and L-type Ca(2+) channel.

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PMID: 11500963

Key Takeaway:

Forskolin is linked to significant increases in testosterone production in Leydig cell studies.

Body Composition and Hormonal Adaptations Associated with Forskolin Consumption in Overweight and Obese Men

Michael P. Godard, Brad A. Johnson, Scott R. Richmond

First published: August 2005 Full publication history

DOI: 10.1038/oby.2005.162 View/save citation

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Abstract

Objective: This study examined the effect of forskolin on body composition, testosterone, metabolic rate, and blood pressure in overweight and obese (BMI ≥ 26 kg/m^2) men.

Research Methods and Procedure: Thirty subjects (forskolin, n = 15; placebo, n = 15) were studied in a randomized, double-blind, placebo-controlled study for 12 weeks.

Results: Forskolin was shown to elicit favorable changes in body composition by significantly decreasing body fat percentage (BF%) and fat mass (FM) as determined by DXA compared with the placebo group ($p \leq 0.05$). Additionally, forskolin administration resulted in a change in bone mass for the 12-week trial compared with the placebo group ($p \leq 0.05$). There was a trend toward a significant increase for lean body mass in the forskolin group compared with the placebo group ($p = 0.097$). Serum free testosterone levels were significantly increased in the forskolin group compared with the placebo group ($p \leq 0.05$). The actual change in serum total testosterone concentration was not significantly different among groups, but it increased 16.77 ± 33.77% in the forskolin group compared with a decrease of 1.08 ± 18.35% in the placebo group.

Discussion: Oral ingestion of forskolin (250 mg of 10% forskolin extract twice a day) for a 12-week period was shown to favorably alter body composition while concurrently increasing bone mass and serum free testosterone levels in overweight and obese men. The results indicate that forskolin is a possible therapeutic agent for the management and treatment of obesity.

Key Takeaway:

Forskolin supplementation at 250mg/day was able to increase T production by 33%.

Boron:

The effect of boron supplementation on the distribution of boron in selected tissues and on testosterone synthesis in rats

M.R. Naghii, S. Samman

Abstract

Boron has been shown to increase the concentration of oestrogen and testosterone in plasma. The aim of this study was to investigate further the effect of boron by determining the response to three levels of boron intake during an experimental period of 6 weeks. The concentration of plasma testosterone and its production in the testes were determined in addition to the distribution of boron in selected tissues. Boron was added to the drinking water as boric acid to provide 2, 12.5, and 25 mg boron/rat/d. Body weight gain was found to be higher at the lowest dose but no significant change was observed at the highest dose. The distribution of boron in all tissues reflected its level of intake with all tissues demonstrating an increase over time. Within 6 weeks, rats fed the lowest and intermediate doses appeared to have a favorable effect on the indices examined, whereas the toxic testicular effects indicated by significant increases in the plasma follicle stimulating hormone concentration and testicular atrophy was associated with the higher dose (25 mg). The synthesis of testosterone by the testicular homogenates *in vitro* from its immediate precursor, androstenedione in the presence of boron was determined, but there did not appear to be any clear relationship between dietary boron and testosterone production in vitro. The effect of boron on steroidogenesis and testicular function and development appears to be proportional to the dose and subsequent boron concentration in the testes.

Key Takeaway:

Boron has been found to dose-dependently increase testosterone levels.

J Trace Elem Med Biol. 2011 Jan;25(1):54-8. doi: 10.1016/j.jtemb.2010.10.001. Epub 2010 Dec 3.

Comparative effects of daily and weekly boron supplementation on plasma steroid hormones and proinflammatory cytokines.

Naghii MR[1], Mofid M, Asgari AR, Hedayati M, Daneshpour MS.

Author information

Abstract

Boron possesses widespread properties in biochemistry and nutrition. Acute supplementation with 11.6 mg of boron resulted in a significant increase in plasma boron concentration. Given such a fast bioavailability, the objective was to determine whether acute (hourly or daily), and weekly supplementation could have any significant biological effects on the steroid hormones and further on some inflammatory biomarkers. Eight healthy male volunteers attended the laboratory on three occasions (days 0, 1 and 7). On the first day (day 0), a blood sample collection at 8.00 A.M was followed by ingestion of placebo with the breakfast. On the next day (supplementation-day 1), similar procedure was followed by ingestion of a capsule containing 10mg of boron. On both occasions blood was collected every 2h for the next 6h. Subjects were requested to consume a capsule of 10mg boron every day with their breakfast, and on the day 7, the blood collection was carried out at 8.00 A.M, again. Boron in plasma increased significantly following hours and weekly consumption. Six hours supplementation showed a significant decrease on sex hormone binding globulin (SHBG), high sensitive CRP (hsCRP) and TNF-α level. After one week (in samples taken at 8.00 A.M, only), the mean plasma free testosterone increased and the mean plasma estradiol decreased significantly. Dihydrotestosterone, cortisol and vitamin D was elevated. Also, concentrations of all three inflammatory biomarkers decreased after supplementation. Of note, despite decreased proinflammatory cytokines, based on recent clinical data, this must be the first human study report to show an increase level of free testosterone after boron consumption.

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PMID: 21129941 DOI: 10.1016/j.jtemb.2010.10.001

[PubMed - indexed for MEDLINE]

Key Takeaway:

Boron supplementation at 10mg/day for 7 days in humans was able to increase free testosterone by 28%, while reducing estrogen by 39% and boosting DHT by 10%.

Inositol:

Endocrinology. 2008 Aug;149(8):3860-9. doi: 10.1210/en.2008-0184. Epub 2008 Apr 24.

Origins of gonadotropin-releasing hormone (GnRH) in vertebrates: identification of a novel GnRH in a basal vertebrate, the sea lamprey.

Kavanaugh SI[1], Nozaki M, Sower SA.

Author information

Abstract

We cloned a cDNA encoding a novel (GnRH), named lamprey GnRH-II, from the sea lamprey, a basal vertebrate. The deduced amino acid sequence of the newly identified lamprey GnRH-II is QHWSHGWFPG. The architecture of the precursor is similar to that reported for other GnRH precursors consisting of a signal peptide, decapeptide, a downstream processing site, and a GnRH-associated peptide; however, the gene for lamprey GnRH-II does not have introns in comparison with the gene organization for all other vertebrate GnRHs. Lamprey GnRH-II precursor transcript was widely expressed in a variety of tissues. In situ hybridization of the brain showed expression and localization of the transcript in the hypothalamus, medulla, and olfactory regions, whereas immunohistochemistry using a specific antiserum showed only GnRH-II cell bodies and processes in the preoptic nucleus/hypothalamus areas. Lamprey GnRH-II was shown to stimulate the hypothalamic-pituitary axis using in vivo and in vitro studies. Lamprey GnRH-II was also shown to activate the inositol phosphate signaling system in COS-7 cells transiently transfected with the lamprey GnRH receptor. These studies provide evidence for a novel lamprey GnRH that has a role as a third hypothalamic GnRH. In summary, the newly discovered lamprey GnRH-II offers a new paradigm of the origin of the vertebrate GnRH family. We hypothesize that due to a genome/gene duplication event, an ancestral gene gave rise to two lineages of GnRHs: the gnathostome GnRH and lamprey GnRH-II.

PMID: 18436713 PMCID: PMC2488216 DOI: 10.1210/en.2008-0184

Key Takeaway: Inositol is needed for the natural synthesis of GnRH (LH, T precursor hormone).

L-Theanine:

J Neurophysiol. 2010 Mar;103(3):1375-84. doi: 10.1152/jn.00910.2009. Epub 2010 Jan 13.

Excitatory action of GABA in the terminal nerve gonadotropin-releasing hormone neurons.

Nakane R[1], Oka Y.

Author information

Abstract

The terminal nerve (TN)-gonadotropin-releasing hormone (GnRH) neurons have been suggested to function as a neuromodulatory system that regulates the motivational and arousal state of the animal and have served as a model system for the study of GnRH neuron physiology. To investigate the synaptic control of the TN-GnRH neurons, we analyzed electrophysiologically the effect of GABA on the TN-GnRH neurons. GABA generally hyperpolarizes most of the neurons in the adult brain by activating GABA(A) receptors while the activation of GABA(A) receptors depolarizes some specific neurons in the mature brain. Here we examined the GABA(A) receptor-mediated responses in the TN-GnRH neurons of adult teleost fish, the dwarf gourami, by means of gramicidin-perforated patch-clamp and cell-attached patch-clamp recordings. The reversal potential for the currents through GABA(A) receptors under the voltage clamp was depolarized relative to the resting membrane potential. GABA(A) receptor activation depolarized TN-GnRH neurons under the current clamp and had excitatory effect on their electrical activity, whereas the stronger GABA(A) receptor activation had bidirectional effect (excitatory-inhibitory). This excitatory effect is suggested to arise from high [Cl(-)](i) and was shown to be suppressed by bumetanide, the blocker of Cl(-)-accumulating sodium-potassium-2-chloride co-transporter (NKCC). The present results demonstrate that GABA(A) receptor activation induces excitation in TN-GnRH neurons, which may facilitate their neuromodulatory functions by increasing their spontaneous firing frequencies. The excitatory actions of GABA in the adult brain have recently been attracting much attention, and the easily accessible large TN-GnRH neurons should be a nice model system to analyze their physiological functions.

PMID: 20071623 DOI: 10.1152/jn.00910.2009

Key Takeaway:

L-theanine stimulates GABA neurons which increases GnRH release naturally.

Glycine:

Amino Acid Neurotransmission and Initiation of Puberty: Evidence from Nonketotic Hyperglycinemia in a Female Infant and Gonadotropin-Releasing Hormone Secretion by Rat Hypothalamic Explants

Jean-Pierre Bourguignon, Jaak Jaeken, Arlette Gerard, and Francis de Zegher

Address all correspondence and requests for reprints to: Prof. J. P. Bourguignon, Division of Pediatric and Adolescent Medicine, University of Liege, Centre Hospitalier Universitaire Sart Tilman, B-4000 Liege, Belgium.

Abstract

The pulse frequency of hypothalamic GnRH secretion increases at the onset of puberty. In rodents and primates, this process involves facilitatory and inhibitory effects mediated through hypothalamic *N*-methyl-D-aspartic acid (NMDA) andγ -aminobutyric acid (GABA) receptors, respectively. Precocious puberty was observed in an 11-month-old girl with nonketotic hyperglycinemia. This was thought to result from the effect of high concentrations of glycine (112 µmol/L in cerebrospinal fluid; normal, 3–12) acting on NMDA receptors as a coagonist of glutamate. Regression of pubertal development during anticonvulsive treatment with GABA agonists (loreclezole and vigabatrin) suggested that the stimulatory effects of glycine could be overcome by GABA receptor-mediated inhibition. These two hypotheses were tested in the *in vitro* model of the explanted hypothalamus from infantile (15-day-old) male rats. Glycine concentrations of 1–10 µmol/L increased the pulse frequency of GnRH secretion. This acceleration was prevented by 7-chlorokynurenic acid, a glycine antagonist at the NMDA receptor complex, and by the GABA agonist loreclezole. In addition, loreclezole and vigabatrin suppressed the developmental increase in the frequency of pulsatile GnRH secretion. The observation of precocious puberty in an infant with hyperglycinemia followed by pubertal regression during GABA agonist therapy and the *in vitro* findings in hypothalamic explants suggest that stimulatory inputs mediated through NMDA receptors and inhibitory inputs through GABA receptors are involved in the initiation of puberty.

Key Takeaway:

Glycine increases the pulsatile release of GnRH in the brain, leading to increases in LH and testosterone production.

Black Pepper Fruit Extract:

The Effect of Fruit Extracts of Black Pepper on the Fertility Potential of Male Albino Mice

Sutyarso[1], **Muhartono**[2], **M. Kanedi**[3],

[1]Department of of Biology, Faculty of Mathematics and Sciences, University of Lampung, Indonesia

[2]Department of Anatomical Pathology, Faculty of Medicine, University of Lampung, Indonesia

[3]Department of Biology, Faculty of Mathematics and Sciences, University of Lampung, Indonesia

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Abstract

This study aimed to determine the effects of black pepper fruit extract on serum testosterone status and fertility potential in male subjects. Twenty seven healthy male mice, four months old, weighing between 25-30 g, were used as experimental animals and grouped into three. The first group was given pellets that do not contain black pepper extract as the control. The second and third groups, respectively were treated with pellets containing water extract and ethanolic extract. Pellets given ad libitum every day for 90 days. Serum testosterone measured by radioimmunoassay (RIA) techniques. Left testis of mice removed, weighed and dissected. Cauda epididymis was separated from testis and squeezed to determine epididymal sperm concentration, motility, and morphology. To determine the diameter of the seminiferous tubules, the number of spermatocytes and spermatids, testes were fixed in Bouin solution, processed and cut at a thickness of 5 um, stained with hematoxylin and eosin and examined under a light microscope at 400x magnification. When compared with control group, male mice treated with fruit extract of black pepper showed significant increase in the serum testosterone level, epididymal sperm concentration, spermatocyte counts, spermatid counts, and the weight of epididymis tubules. As the conclusion, fruit extract of black pepper has a positive effect on androgenic hormone level and fertility potential in male mice.

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Key Takeaway:

Has potential for increasing androgenic hormone production.

Research Highlights

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Key Takeaway:

Black pepper fruit extract has been shown to significantly increase the absorption of ingredients in supplements.