Effect of herbal extract mixture on menopausal urinary incontinence in ovariectomized rats.

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Abstract
The decline of estrogen production after menopause is contributing factor to urinary incontinence (UI), and particularly stress urinary incontinence (SUI). We determined the preventive effects of herbal extract mixture (HEM) on UI in ovariectomized Sprague Dawley rats. Female 9-weeks old rats were ovariectomized and treated with HEM (2.2, 11, or 55 mg/kg/day) for 8 weeks. The index of urinary bladder weight to body weight in the HEM and non-ovariectomized and non-treated (SHAM) groups were slightly higher than the ovariectomized, non-treated group (OVX). The contraction index of acetylcholine to KCl on detrusor smooth muscle strips in the HEM groups showed a dose-dependent recovery. HEM treatment also significantly improved collagen levels, as shown by Masson trichrome staining, as well as hydroxyproline levels in the urinary bladder. Serum estradiol levels in the HEM groups were higher than the OVX group. In conclusion, HEM increased estradiol levels in serum and improved factors related to urinary incontinence. The improvements in estradiol levels were related to changes in urinary incontinence.

PMID: 16971748 [PubMed - indexed for MEDLINE]
Serenoa repens


**Extracts from fruits of saw palmetto (Sabal serrulata) and roots of stinging nettle (Urtica dioica): viable alternatives in the medical treatment of benign prostatic hyperplasia and associated lower urinary tracts symptoms.**

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**Abstract**

Benign prostatic hyperplasia (BPH) and associated lower urinary tract symptoms (LUTS) are very common disorders in aging men. Despite the great clinical importance, many aspects of their aetiology remain uncertain although it is generally accepted that advanced age and testicular androgens are important requirements for the development of these complaints. The currently available therapeutic options include watchful waiting, changes of life style, medical treatments and invasive therapies. In many European countries the use of phytopharmaceuticals for the management of BPH and related LUTS is common and these products represent up to 80% of all drugs prescribed for this disorder. In particularly, extracts from the fruits of saw palmetto (Sabal serrulata, syn. Serenoa repens) and the roots of stinging nettle (Urtica dioica) are popular. During the last years numerous papers have been published which elaborated on the pharmacological activities and the clinical assessment of these herbal remedies. These investigations have not only broadened the scientific basis for the rational use of phytotherapeutics but have also provided evidence for their therapeutic efficacy and favourable safety profile.

PMID: 11509966 [PubMed - indexed for MEDLINE]

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Abstract

OBJECTIVES: Permixon is a compound extracted from the fruit of the American dwarf palm tree, Serenoa repens. Controversy regarding the use of phytotherapeutic agents in men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia is significant. We analyzed all available clinical trial data of the Permixon preparation to determine its clinical efficacy compared with placebo.

METHODS: All published clinical trial data on Permixon (11 randomized clinical trials and 2 open label trials), involving 2859 patients, were used. These trials were disparate in size (from 22 to 592 patients) and duration (from 21 to 180 days). Peak urinary flow rate and nocturia were the two common end points. The statistical analysis was based on a random effects meta-analysis.

RESULTS: The average +/- SE placebo effect on the peak urinary flow rate was an increase of 0.51 +/- 0.51 mL/s. The estimated effect of Permixon was a further increase of 2.20 +/- 0.51 mL/s (P <0.001).
Placebo was associated with a reduction in the mean number +/- SE of nocturnal urinations of 0.69 +/- 0.15. A further reduction of 0.50 +/- 0.01 episodes of urination (P <0.001) occurred that was attributable to Permixon. Some heterogeneity was found among the studies. Treatment duration did not appear to impact either of these effects.

CONCLUSIONS: This meta-analysis of all available published trials of Permixon in the treatment of men with benign prostatic hyperplasia revealed a significant improvement in peak flow rate and reduction in nocturia greater than with placebo.
Abstract

Serenoa repens (Permixon) has been available for several years for the treatment of men with benign prostatic hyperplasia (BPH). The drug is the n-hexane lipidosterolic extract of the dwarf American palm (also known as Serenoa repens) and is a complex mixture of various compounds. A number of pharmacodynamic effects have been demonstrated with the lipidosterolic extract of Serenoa repens (LSES), suggesting multiple mechanisms of action including in vitro inhibition of both type 1 and type 2 isoenzymes of 5 alpha-reductase and interference with binding of dihydrotestosterone to cytosolic androgen receptors in prostate cells. In controlled clinical trials in men with BPH, oral administration of Serenoa repens 160 mg twice daily for 1 to 3 months was generally superior to placebo in improving subjective symptoms, such as dysuria, as well as objective parameters. The frequency of nocturia was reduced by 33 to 74%, while urinary frequency during the day decreased by 11 to 43% and peak urinary flow rate increased by 26 to 50% with Serenoa repens. Corresponding values for placebo were 13 to 39%, 1 to 29% and 2 to 35%. The only large comparative trial conducted to date, in which > 1000 men with moderate BPH were randomised to receive Serenoa repens 160 mg twice daily or finasteride 5 mg once daily for 6 months, demonstrated similar efficacy between the two drugs. No statistically significant difference was demonstrated between treatment groups for improvement in patient self-rated quality-of-life scores and the primary end-point of objective symptom score; International Prostate Symptom Score improved by 37% with Serenoa repens compared with 39% with finasteride. In much smaller comparative trials, few significant differences were demonstrated between Serenoa repens and alpha 1-receptor antagonists, and larger randomised trials of adequate duration are required to better compare the clinical efficacy of these drugs. The most frequently reported adverse events in clinical trials with Serenoa repens have been minor gastrointestinal problems (e.g. nausea and abdominal pain). In conclusion, Serenoa repens is well tolerated and has greater efficacy than placebo and similar efficacy to finasteride in improving symptoms in men with BPH. Although there is a need for further comparative studies, particularly with alpha 2-receptor antagonists, available data indicate that Serenoa repens is a useful alternative to alpha 1-receptor antagonists and finasteride in the treatment of men with BPH.
Botanical medicines for the urinary tract.

Yarnell E.

Abstract

Four important categories of urologic herbs, their history, and modern scientific investigations regarding them are reviewed. Botanical diuretics are discussed with a focus on Solidago spp (goldenrod) herb, Levisticum officinale (lovage) root, Petroselinum crispus (parsley) fruit, and Urtica dioica (stinging nettle) herb. Urinary antiseptic and anti-adhesion herbs, particularly Arctostaphylos uva-ursi (uva-ursi) leaf, Juniperus spp (juniper) leaf, and Vaccinium macrocarpon (cranberry) fruit are reviewed. The antinephrotoxic botanicals Rheum palmatum (Chinese rhubarb) root and Lespedeza capitata (round-head lespedeza) herb are surveyed, followed by herbs for symptoms of benign prostatic hyperplasia, most notably Serenoa repens (saw palmetto) fruit, Urtica dioica root, and Prunus africana (pygeum) bark.

PMID: 12522584 [PubMed - indexed for MEDLINE]
Phytotherapy in the treatment of benign prostatic hyperplasia.

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Abstract
There are numerous plant extracts that have been used for the treatment of benign prostatic hyperplasia and lower urinary tract symptoms. While some extracts show promise, their efficacy has not been adequately proven in long-term, double-blind placebo-controlled trials monitored by an outside agency.

PMID: 11753128 [PubMed - indexed for MEDLINE]
Phytotherapeutic agents in the treatment of benign prostatic hyperplasia.

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Abstract

The rationale and efficacy of phytotherapeutic agents in the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia (BPH) are continuously debated. While plant extracts are prescribed and reimbursable treatment options in Europe, they are officially classified merely as dietary supplements in the United States. The most commonly used preparations originate from the species Serenoa repens, Pygeum africanum, hypoxis rooperi, pinus, picea, urtica dioica, and secale cereale. Combination extracts derived from two or more plants are also used. Various components have been suggested to be active, and different mechanisms of action are being supposed. Open trials and some short-term randomized studies, suggesting safety and efficacy, have been reported. However, if stringent criteria of evidence-based medicine are applied, the data are inconclusive. Therefore, the 4th International Consultation on BPH and the recent German guidelines have not (yet) recommended phytotherapy for the management of symptomatic BPH.

PMID: 12084323 [PubMed - indexed for MEDLINE]
Abstract

The oil from the pumpkin (Cucurbita pepo) seed is claimed to be useful in the management of benign prostatic hyperplasia. This investigation seeks to examine the effect of pumpkin seed oil on testosterone-induced hyperplasia of the prostate of rats. Hyperplasia was induced by subcutaneous administration of testosterone (0.3 mg/100 g of body weight) for 20 days. Simultaneous oral administration of either pumpkin seed oil (2.0 and 4.0 mg/100 g of body weight) or corn oil (vehicle) was also given for 20 days. The weights of the rats were recorded weekly, and the influence of testosterone and pumpkin seed oil on the weight gain of the rats was examined. On day 21, rats were sacrificed, and the prostate was removed, cleaned, and weighed. The prostate size ratio (prostate weight/rat body weight) was then calculated. Neither testosterone nor pumpkin seed oil had any significant influence on the weight gain of the rats. Testosterone significantly increased prostate size ratio (P < .05), and this induced increase was inhibited in rats fed with pumpkin seed oil at 2.0 mg/100 g of body weight. The protective effect of pumpkin seed oil was significant at the higher pumpkin seed oil dose (P < .02). We conclude pumpkin seed oil can inhibit testosterone-induced hyperplasia of the prostate and therefore may be beneficial in the management of benign prostatic hyperplasia.

PMID: 16822218 [PubMed - indexed for MEDLINE]
Abstract

Extracts from Pygeum africanum, Serenoa repens and Cucurbita pepo are used in the treatment of benign prostatic hyperplasia (BPH) and prostate cancer (PCa). The activity of the androgen receptor (AR) is known to control growth of the prostate. Here, we examined extracts of these plants for their antiandrogenic activity using an AR responsive reporter gene assay for drug discovery. A selective dichloromethane extract from the stem barks of Pygeum africanum revealed the highest antiandrogenic effect. Bioactivity-directed fractionation of this extract led to the isolation of N-butylbenzenesulfonamide (NBBS) indicating that extracts of the stem bark of P. africanum harbour androgen antagonistic activity. This compound may provide a novel approach for the prevention and treatment of BPH and human PCa.

PMID: 16783690 [PubMed - indexed for MEDLINE]
Rehmannia glutinosa


Rehmannia glutinosa ameliorates the progressive renal failure induced by 5/6 nephrectomy.

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Abstract

AIM OF THE STUDY: Rehmannia glutinosa, the steamed root of the Scrophulariaceae family, has been widely used in Asian countries for the treatment of renal diseases. In this study, we evaluated the renoprotective effect of aqueous extract of Rehmannia glutinosa in progressive renal failure.

MATERIALS AND METHODS: The effects of Rehmannia glutinosa on renal function, 24-h proteinuria, and the expression of angiotensin II, angiotensin II type 1 (AT(1)) receptor, TGF-beta1, and type IV collagen in renal cortex were analyzed in progressive renal failure rats induced by 5/6 nephrectomy.

RESULTS: Rehmannia glutinosa reduced the serum creatinine level, 24-h urinary protein excretion, and glomerulosclerosis, and it also inhibited the expression of angiotensin II, AT(1) receptor, TGF-beta1 and type IV collagen in the renal cortex.

CONCLUSIONS: These results suggest that the renoprotective effect of Rehmannia glutinosa might be mediated by suppressing the expression of angiotensin II and AT(1) receptor and by regulating TGF-beta1 and type IV collagen expression.
Ethanol extracts of Rehmannia complex (Di Huang) containing no Corni fructus improve early diabetic nephropathy by combining suppression on the ET-ROS axis with modulate hypoglycemic effect in rats.

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Abstract

AIM: Liuwei Dihuang (Rehmannia complex, RC) decoction, a classic prescription of Traditional Chinese Medicine (TCM), has been used in treating diabetic nephropathy (DN). Among the 6 crude medicines which contains Corni fructus is recognized as the active fraction for its effectiveness. We aimed to investigate, first, if without Corni fructus a modified RC could be still effective, second, if the ethanol extracts could be better than that of water extract and third, the beneficial effect is mainly stemmed from suppressing the endothelin (ET-1) pathway associated with a moderate hypoglycemic effect.

METHODS AND MATERIALS: Diabetes for 8 weeks was induced by a single dose of streptozotocin (STZ, 65 mg/kg, i.p.) in rats and treated with RC extracts in either 95%, 70% ethanol or water separately during 5-8th week. The efficacy of extracts was compared with aminoguanidine (AMG).

RESULTS: An increase in albumin and creatinine in 24h urine, blood urea nitrogen (BUN) was found in STZ rats. Oxidative stress was found in renal cortex in association with upregulated plasma ET-1 and mRNA of ETA, decreased MMP 2,9 (matrix matelloproteinases) and increased hydroxyproline.

CONCLUSIONS: The RC without Corni fructus was very effective in alleviating DN and ethanol extracts provided greater effects against water extracts. The efficacy in alleviating DN is attributed to normalizing the activated ET system, oxidative stress and MMP 2,9 in combination with a moderate hypoglycemic activity.
Rehmannia glutinose ameliorates renal function in the ischemia/reperfusion-induced acute renal failure rats.

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Abstract

The present study was designed to examine whether aqueous extract of steamed root of Rehmannia glutinose (ARR) has an ameliorative effect on renal functional parameters in association with the expressions of aquaporin 2 (AQP 2), Na,K-ATPase, and heme oxygenase-1 (HO-1) in the ischemia-reperfusion induced acute renal failure (ARF) rats. Polyuria caused by down-regulation of renal AQP 2 in the ischemia-induced ARF rats was markedly restored by administration of ARR (200 mg/kg, p.o.) with restoring expression of AQP 2 in the kidney. The expressions of Na,K-ATPase alpha1 and beta1 subunits in the renal medullar and cortex of the ARF rats were also restored in the ARF rats by administration of ARR. On the other hand, administration of ARR lowered the renal expression of HO-1 up-regulated in rats with ischemia-induced ARF. The renal functional parameters including creatinine clearance, urinary sodium excretion, urinary osmolality, and solute-free reabsorption were also markedly restored in ischemia-ARF rats by administration of ARR. Taken together, these data indicate that RSR ameliorates renal defects in rats with ischemia-induced ARF.

PMID: 16141536 [PubMed - indexed for MEDLINE]
Clinical study on treatment of mid-advanced crescentic nephritis by qingre huoxue recipe

[Article in Chinese]

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Abstract

OBJECTIVE: To evaluate the therapeutic effect of integrative Chinese and Western medicine in treating mid-advanced crescentic nephritis (MACN).

METHODS: Thirty-two patients, their diagnosis was confirmed as MACN by renal biopsy, were divided, adopting randomized, controlled method, into two groups, the treated group and the control group, they were all, excepting one, treated with impact therapy of methyl-prednisolone followed with oral intake of prednisone, to part of them cyclophosphamide or mycophenolate mofetil was given in addition, to those with hypo-hemoglobin (< 90 g/L), subcutaneous injection of erythropoietin was administered. Decoction of Qingre Huoxue recipe (QHR), consisted of oldenlandia herb 30 g, honey-suckle stem 30 g, violet herb 30 g, red peony root 15 g, rehmannia root 15 g, solomonseal rhizome 15 g, asiabell root 30 g, red sage root 30 g, prepared rhubarb 12 g and giant-hyssop herb 12 g, were additionally given one dose per day to patients in the treated group. The renal function, improvement of anemia and immunosuppressive agents needed in patients were observed after 3 months treatment.

RESULTS: After treatment, renal function was improved in both groups, but the effect in the treated group was better than that in the control group (P < 0.05). Anemia was partially alleviated in the two groups with no significant difference. The dosage of glucocorticoids used in the treated group was obviously lesser than that used in the control group (P < 0.01).

CONCLUSION: Integrative Chinese and western medicine could treat crescentic nephritis to obtain good effect, and reduce the quantity of glucocorticoid necessity for treatment.
Amelioration of diabetic nephropathy by dried Rehmanniae Radix (Di Huang) extract.

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Abstract

The effects of dried Rehmanniae Radix (Di Huang) extract were investigated using a diabetic nephropathy model: rats given streptozotocin after nephrectomy. The results showed that this crude drug reduced the magnitudes of the increases in glucose, urea nitrogen, 5-hydroxymethylfurfural and thiobarbituric acid (TBA)-reactive substance levels, with the effects being most marked in the high blood glucose group. The renal histopathological lesions, which were conspicuous in rats not given dried Rehmanniae Radix extract, were ameliorated considerably in the high blood glucose group given this extract. It appears that dried Rehmanniae Radix extract may be useful as a therapeutic agent for inhibiting the progression of diabetic nephropathy. On the basis of these results, the possible mechanisms of action of this crude drug are discussed.

PMID: 15673189 [PubMed - indexed for MEDLINE]
Clinical and experimental study on effects of man-shen-ling oral liquid in the treatment of 100 cases of chronic nephritis

[Article in Chinese]

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Abstract

A new Chinese herbal preparation, Man-Shen-Ling (MSL, consisted of medicinal herbs such as Astragalus and Rehmannia) in treating 100 cases of chronic nephritis. The effective rate was 91% in comparing to 66.7% in the control group, P < 0.001. It was markedly effective for proteinuria, hematuria, improvement and recovery of renal functions, edema, anemia, anorexia etc in comparing with the control group. It showed no adverse effects on functions of liver, kidney, heart and GI tract. Animal model of chronic nephritis was established and the effects of MSL were observed. The laboratory findings and histopathological investigation on kidney revealed and confirmed that MSL has therapeutic effects on chronic nephritis. Pharmacodynamically, MSL exhibited effects of anti-allergy, its immuno-suppressive effect corresponded to that of cyclophosphamide, with diuretic, hypotensive, proteinuria eliminating, anti-inflammatory, anti-coagulatory, renal blood flow and glomerular filtration enhancing, the excretion of urea-nitrogen, potassium and sodium promoting function; in addition, it also could promote and modulate the immunity. Acute and chronic toxicity tests on animal models neither showed toxic, mutagenic, teratogenic nor carcinogenic effects. It is a new preparation of Chinese medicinal herbs in treating chronic nephritis, it is safe and effective.

PMID: 8219675 [PubMed - indexed for MEDLINE]
Olea europaea


Antioxidant capacity of 55 medicinal herbs traditionally used to treat the urinary system: a comparison using a sequential three-solvent extraction process.

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Abstract

BACKGROUND: The prevalence of chronic renal disease exceeds 10% in industrialized societies. Oxidative damage is thought to be one of the main mechanisms involved in nearly all chronic renal pathologies.

OBJECTIVE: We aimed to use the oxygen radical absorbance capacity (ORAC) method and a sequential multisolvent extraction process to compare the in vitro antioxidant capacity of 55 medicinal herbs and prioritize them for in vivo studies investigating the value of herbal therapies in the treatment of renal disorders.

METHODS: The herbs were chosen on the basis of their traditional use in kidney or urinary system disorders, or because they have attracted the attention of recent investigations into renal pathologies. The three solvents used for extraction were ethyl acetate, methanol, and 50% aqueous methanol. Silybum marianum (milk thistle) seed and Camellia sinensis (tea) leaf, both known to possess high antioxidant capacity, were included for comparison.

RESULTS: Twelve of the 55 herbs were comparable to or exceeded ORAC levels of milk thistle seed or tea leaf. The highest radical-scavenging activity was found in Olea europaea (olive leaf), Cimicifuga racemosa (black cohosh), Rheum palmatum (rhubarb), Glycyrrhiza glabra (licorice), and Scutellaria lateriflora (Virginia skullcap).

CONCLUSIONS: The antioxidant capacity of many of the herbs studied may, at least in part, be responsible for their reputation as being protective of organs of the urinary system. Overall, the combined ORAC values for the methanol and aqueous methanol extracts comprised 84% of the total ORAC value. Sequential extraction with solvents of different polarities may be necessary to fully extract the antioxidant principles from medicinal plants.

PMID: 17309384 [PubMed - indexed for MEDLINE]
Zea mays


[An orientational examination of the effects of extracts from mixtures of herbal drugs on selected renal functions]

[Article in Czech]
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Abstract
The paper aimed to determine the effects of mixtures of selected medicinal plants on some physiological renal functions, i.e. excretion of urine and electrolytes and changes in the quantity of prostaglandins E2 (PGE2) and kallikrein-kinins in rat blood plasma after water and salt load. The following medicinal plants were selected for the examination: downy birch (Betulae pubescens EHRH.), everlasting flower (Helichrysum arenarium L. MOENCH.), hawthorn (Crataegus oxyacantha L.), woodland strawberry (Fragaria vesca L.), sweet corn (Zea mays L.), German chamomile (Matricariae recutita L.), and field horsetail (Equiseti arvense L.). Herbal drugs were used to compose 6 mixtures. Extracts from these mixtures were administered to Wistar strain males and their effects were compared with the effects of an administered suspension of hydrochlorothiazide, an extract from field horsetail herb alone, and a control group of animals which was not administered any preparation. The greatest diuretic effect was found in a mixture composed of birch leaves (Betulae folium), hawthorn berries (Crataegi fructus), strawberry leaves (Fragariae folium), corn silk (Maydis stigmata), chamomile flowers (Matricariae flos), and horsetail herb (Equiseti herba). Its effect was greater by 47% and 34% than the effect of a horsetail herb extract and a hydrochlorothiazide suspension (p < 0.05), respectively. The extract from this mixture also increased the quantity of prostaglandins E2 and kallikrein-kinins in rat blood plasma in water and salt load.

PMID: 17619305 [PubMed - indexed for MEDLINE]
Zea mays L. extracts modify glomerular function and potassium urinary excretion in conscious rats.

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Abstract
Diuretic and uricosuric properties have traditionally been attributed to corn silk, stigma/style of Zea mays L. Although the diuretic effect was confirmed, studies of the plant's effects on renal function or solute excretion were lacking. Thus, we studied the effects of corn silk aqueous extract on the urinary excretion of water, Na+, K+, and uric acid. Glomerular and proximal tubular function and Na+ tubular handling were also studied. Conscious, unrestrained adult male rats were housed in individual metabolic cages (IMC) with continuous urine collection for 5 and 3 h, following two protocols. The effects of 25, 50, 200, 350, and 500 mg/kg body wt. corn silk extract on urine volume plus Na+ and K+ excretions were studied in water-loaded conscious rats (2.5 ml/100 g body wt.) in the IMC for 5 h (Protocol 1). Kaliuresis was observed with doses of 350 (100.42 +/- 22.32-120.28 +/- 19.70 microEq/5 h/100 g body wt.; n = 13) and 500 mg/kg body wt. (94.97 +/- 29.30-134.32 +/- 39.98 microEq/5h/100 g body wt.; n = 12; p<0.01), and the latter dose resulted in diuresis as well (1.98 +/- 0.44-2.41 +/- 0.41 ml/5 h/100 g body wt.; n = 12; p<0.05). The effects of a 500 mg/kg body wt. dose of corn silk extract on urine volume plus Na+ and K+ excretions were studied in water-loaded conscious rats (2.5 ml/100 g body wt.) in the IMC for 5 h (Protocol 1). Kaliuresis was observed with doses of 350 (100.42 +/- 22.32-120.28 +/- 19.70 microEq/5 h/100 g body wt.; n = 13) and 500 mg/kg body wt. (94.97 +/- 29.30-134.32 +/- 39.98 microEq/5h/100 g body wt.; n = 12; p<0.01), and the latter dose resulted in diuresis as well (1.98 +/- 0.44-2.41 +/- 0.41 ml/5 h/100 g body wt.; n = 12; p<0.05). The effects of a 500 mg/kg body wt. dose of corn silk extract on urine volume, Na+, K+ and uric acid excretions, and glomerular and proximal tubular function, were measured respectively by creatinine (Clcr) and Li+ (ClLi) clearances and Na+ tubular handling, in water-loaded rats (5 ml/100 g body wt.) in the IMC for 3 h (Protocol 2). Clcr (294.6 +/- 73.2, n = 12, to 241.7 +/- 48.0 microl/ min/100 g body wt.; n = 13; p<0.05) and the Na+ filtered load (41.9 +/- 10.3, n = 12, to 34.3 +/- 8, n = 13, p<0.05) decreased and ClLi and Na+ excretion were unchanged, while K+ excretion (0.1044 +/- 0.0458, n=12, to 0.2289 +/- 0.0583 microEq/min/100 body wt.; n = 13; p<0.01) increased. For Na+ tubular handling, the fractional proximal tubular reabsorption (91.5 +/- 3.5, n = 12, to 87.5 +/- 3.4%; n = 13; p<0.01) decreased, and both fractional distal reabsorptions--I and II--increased (96.5 +/- 1.5, n = 12, to 97.8 +/- 0.9%; n = 13; p<0.01; and 8.2 +/- 3.5, n = 12, to 12.2 +/- 3.4%, n = 13, p<0.01, respectively). To summarize, in water-loaded conscious rats (2.5 ml/100 body wt.), corn silk aqueous extract is diuretic at a dose of 500 mg/kg body wt. and kaliuretic at doses of 350 and 500 mg/kg body wt. In water-loaded conscious rats (5.0 ml/100 g body wt.), corn silk aqueous extract is kaliuretic at a dose of 500 mg/kg body wt., but glomerular filtration and filtered load decrease without affecting proximal tubular function, Na+, or uric acid excretion.

PMID: 15957371 [PubMed - indexed for MEDLINE]
Abstract

OBJECTIVES: Tribulus terrestris L. (Zygophyllaceae) which is called Al-Gutub (in Iraqi dialect) or Quti;ba (in classical Arabic medicine), and Zea mays were both used alone or in combination by Iraqi herbalists to propel urinary stones. We studied the aqueous extract of the leaves and fruits of T. terrestris and the hair of Z. mays, to determine their diuretic activity and the contractile effect of T. terrestris.

METHODS: The aqueous extract was filtered and the solvent was evaporated to produce a dry crude extract. The dry extract was then dissolved in physiological saline to make the required concentrations. Wistar male rats were used for the diuresis test and strips of isolated Guinea pig ileum were used for the contractility test.

RESULTS: The aqueous extract of T. terrestris, in oral dose of 5g/kg elicited a positive diuresis, which was slightly more than that of furosemide. Z. mays aqueous extract did not result in significant diuresis when given alone in oral dose of 5g/kg, while combination of Z. mays and T. terrestris extracts produced the same extent of diuresis as that produced by T. terrestris alone. Na(+), K(+) and Cl(+) concentrations in the urine had also much increased. In addition to its diuretic activity T. terrestris had evoked a contractile activity on Guinea pig ileum.

CONCLUSION: T. terrestris has long been used empirically to propel urinary stones. The diuretic and contractile effects of T. terrestris indicate that it has the potential of propelling urinary stones and merits further pharmacological studies.
Studies on the individual and combined diuretic effects of four Vietnamese traditional herbal remedies (Zea mays, Imperata cylindrica, Plantago major and Orthosiphon stamineus).


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Abstract

Herbal remedies are widely used in Vietnam alongside modern drugs. We assessed the diuretic effect of four traditional Vietnamese herbal remedies from Zea mays, Imperata cylindrica, Plantago major and Orthosiphon stamineus, all claimed to produce an increase of diuresis. No influence was recorded for the 12- and 24-h urine output or on the sodium excretion for any of the drugs when tested under standardized conditions in a placebo controlled double-blind crossover model. The present study indicates the need for critical review of the present recommendations regarding therapy with plant materials in countries relying on empiric traditions.

PMID: 1434681 [PubMed - indexed for MEDLINE]
Vitamina B6 (Piridoxina)


Vitamin B6 and oxalic acid in clinical nephrology.

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Abstract

OBJECTIVE: Vitamin B(6) (VB(6)) is a water-soluble vitamin, which is important for the normal functioning of multiple organ systems. It is metabolized to the active molecule pyridoxal-5-phosphate (PLP). Oxalic acid (OA) is thought to be a uremic toxin that participates in the pathogenesis of the uremic syndrome. The objectives of this study were as follows: (1) to evaluate the plasma and erythrocyte VB(6) (effect of PLP; effect of PLP was in indirect relationship with the concentration of erythrocyte VB(6)), and plasma and urinary OA in marathon runners, in patients with acute intermittent porphyria (AIP) and variegate porphyria, and in patients with stage 1 chronic kidney disease (CKD), chronic glomerulonephritis and nephrotic syndrome (CGNS); (2) to examine the influence of water diuresis in healthy subjects, and the influence of sodium diuresis (high sodium intake) and an intravenous administration of furosemide on the urinary excretion of VB(6) and OA in CKD stage 3-4 patients; and (3) to evaluate the influence of erythropoietin treatment on erythrocyte VB(6) (effect of PLP) in hemodialysis (HD) patients, and the influence of continuous ambulatory peritoneal dialysis (CAPD) therapy on plasma VB(6) and OA and their peritoneal clearance and transfer.

DESIGN AND SETTING: This study was conducted at the Nephrological Clinic of L. Pasteur Faculty Hospital and of Medical School of P. J. Safarik University. A combination of 29 marathon runners, 15 patients with CG and NS, 11 patients with AIP, 1 patient with variegate porphyria, 15 healthy subjects, 27 CKD stage 3-4 patients, 30 HD, and 27 CAPD patients were used in the study.

RESULTS: After a marathon run, plasma and erythrocyte VB(6) significantly decreased and plasma OA increased. Plasma (15.5 +/- 3.8 nmol/L) and erythrocyte VB(6) (effect of PLP: 42.1% +/- 7.5%) were decreased and plasma OA (9.8 +/- 2.3 micromol/L) was significantly elevated in patients with CGNS and stage 1 CKD. In patients with AIP, deficiency of plasma (24.3 +/- 5.2 nmol/L) and erythrocyte VB(6) (effect of PLP: 46.2% +/- 7.0%) and hyperoxalemia (9.39 +/- 2.5 micromol/L) were present. The urinary excretion of VB(6) and of OA during maximal water diuresis and after intravenous administration of furosemide increased significantly (P < .01), but was not affected by the high intake of NaCl (P > .05). Erythropoietin treatment in HD patients led to the erythrocyte VB(6) deficiency. This finding is an indirect evidence that erythrocyte VB(6) is consumed by the hemoglobin synthesis much more during EPO treatment. In CAPD patients, plasma value of VB(6) (127.3 +/- 66.9 micromol/L) was in the normal range and plasma OA (23.6 +/- 7.4 micromol/L) was significantly elevated. Mean value of peritoneal clearance of VB(6) was 8.8% and of OA was 76.9% of urea clearance.

CONCLUSION: Our study indicates that deficiency of VB(6) led to hyperoxalemia and hyperoxaluria in patients with CKD. Deficiency of VB(6) in CKD stage 4-5 patients potentiates the uremic hyperoxalemia and hyperoxaluria.

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Oxalate synthesis from hydroxypyruvate in vitamin-B6-deficient rats.

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Abstract
We studied the effects of an intravenous hydroxypyruvate load on endogenous oxalogenesis in rats receiving a standard diet or a vitamin-B6-deficient diet. Twelve male Wistar rats were randomized to two groups and were fed either a standard diet or a vitamin-B6-deficient diet for 3 weeks. Then the animals received an intravenous infusion of 100 mg/ml (960.6 micromol/ml) of hydroxypyruvate slowly over 10 min. Urine samples were collected just before hydroxypyruvate infusion and at hourly intervals until 5 h afterward. Urinary oxalate, glycolate, and citrate levels were measured by capillary electrophoresis. Hourly urinary oxalate excretion peaked within 2 h, while urinary glycolate excretion peaked at 1 h, after the hydroxypyruvate load in both control and vitamin-B6-deficient rats. Both urinary oxalate and glycolate excretion were higher in vitamin-B6-deficient rats than in control rats. Infusion of hydroxypyruvate increased the 5-h urinary oxalate and glycolate excretion to 0.68% (6.56 micromol) and 0.53% (5.10 micromol) of the administered dose (mol/mol), respectively, in the control rats, while oxalate and glycolate excretion, respectively, increased to 2.43% (23.36 micromol) and 0.79% (7.59 micromol) of the dose in the vitamin-B6-deficient rats. Urinary citrate excretion was significantly lower at baseline and all other times in the vitamin-B6-deficient rats than in the control rats. In conclusion, a hydroxypyruvate load increased endogenous oxalate synthesis in control rats, and its synthesis was even greater in vitamin-B6-deficient rats. Vitamin B6 deficiency also resulted in significant hypocitraturia.

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Vitamin B6 status, deficiency and its consequences--an overview.
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Abstract

BACKGROUND: Vitamin B6 is thought to be a most versatile coenzyme that participates in more than 100 biochemical reactions. It is involved in amino acid and homocysteine metabolism, glucose and lipid metabolism, neurotransmitter production and DNA/RNA synthesis. Vitamin B6 can also be a modulator of gene expression. Nowadays, clinically evident vitamin B6 deficiency is not a common disorder, at least in the general population. Nevertheless, a subclinical, undiagnosed deficiency may be present in some subjects, particularly in the elderly.

OBJECTIVE: This review gives a complete overview over the metabolism and interactions of vitamin B6. Further, we show which complications and deficiency symptoms can occur due to a lack of vitamin B6 and possibilities for public health and supplemental interventions.

METHODS: The database Medline (www.ncvi.nlm.nih.gov) was searched for terms like "vitamin B6", "pyridoxal", "cancer", "homocysteine", etc. For a complete understanding, we included studies with early findings from the forties as well as recent results from 2006. These studies were summarised and compared in different chapters.

RESULTS AND CONCLUSION: In fact, it has been proposed that suboptimal vitamin B6 status is associated with certain diseases that particularly afflict the elderly population: impaired cognitive function, Alzheimer's disease, cardiovascular disease, and different types of cancer. Some of these problems may be related to the elevated homocysteine concentrations associated to vitamin B6 deficiency, but there is also evidence for other mechanisms independent of homocysteine by which a suboptimal vitamin B6 status could increase the risk for these chronic diseases.

PMID: 17260529 [PubMed - indexed for MEDLINE]
Chemoprevention for bladder cancer.

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Abstract

PURPOSE: Bladder cancer is the most expensive cancer to treat and follow in the United States due to often extended courses of treatment coupled with the necessity for frequent surveillance examinations. Because direct exposure to carcinogens is implicated in bladder cancer development and many potentially protective compounds are concentrated in urine, bladder cancer is a logical target for chemoprevention.

MATERIALS AND METHODS: We performed a MEDLINE search of the English language literature to identify reports of chemoprevention of bladder cancer. Study outcomes were evaluated and mechanisms of action were identified when possible. In cases of multiple reports of the same compound critical comparisons were performed.

RESULTS: For most putative chemopreventive agents against bladder cancer the results of different studies are conflicting. Megadose vitamins, certain vitamin A analogues and pyridoxines have been associated with promising findings. For vitamins C and E and selenium, studies showing benefit are balanced by studies showing no benefit. Other compounds, such as soy, green tea and isothiocyanates, have been suggested by some studies to be protective and by others to be tumor promoting.

CONCLUSIONS: For most bladder cancer chemopreventive agents studied to date results regarding efficacy vary, precluding the possibility of universal support by health care providers for this specific role. Megadose multivitamin supplements have demonstrated the ability to prevent bladder cancer recurrences in a single smaller study. Some analogues of vitamins A, B6, C and E have been shown to be beneficial in other disease processes, suggesting that these compounds may be advocated with the caveat that they do not have a specific protective role in bladder cancer. Data from randomized, prospective trials show a benefit in bladder cancer only after eliminating early or initial recurrences, suggesting the need for long-term administration of a chosen agent. Additional prospective trials with long-term followup, likely involving multiple institutions, are required before definitive recommendations can be made about chemoprevention for bladder cancer. In 2006 no oral agent can be recommended and to our knowledge the best chemopreventive strategy remains to be determined.

PMID: 17070211 [PubMed - indexed for MEDLINE]
The vitamins folic acid, B12 and B6 are the source of coenzymes which participate in one carbon metabolism. In this metabolism, a carbon unit from serine or glycine is transferred to tetrahydrofolate (THF) to form methylene-THF. This is either used as such for the synthesis of thymidine, which is incorporated into DNA, oxidized to formyl-THF which is used for the synthesis of purines, which are building blocks of RNA and DNA, or it is reduced to methyl-THF which is used to methylate homocysteine to form methionine, a reaction which is catalyzed by a B12-containing methyltransferase. Much of the methionine which is formed is converted to S-adenosylmethionine (SAM), a universal donor of methyl groups, including DNA, RNA, hormones, neurotransmitters, membrane lipids, proteins and others. Because of these functions, interest in recent years has been growing particularly in the area of aging and the possibility that certain diseases that afflict the aging population, loss of cognitive function, Alzheimer's disease, cardiovascular disease, cancer and others, may be in part explained by inadequate intake or inadequate status of these vitamins. Homocysteine, a product of methionine metabolism as well as a precursor of methionine synthesis, was shown recently to be a risk factor for cardiovascular disease, stroke and thrombosis when its concentration in plasma is slightly elevated. There are now data which show association between elevated plasma homocysteine levels and loss of neurocognitive function and Alzheimer's disease. These associations could be due to a neurotoxic effect of homocysteine or to decreased availability of SAM which results in hypomethylation in the brain tissue. Hypomethylation is also thought to exacerbate depressive tendency in people, and for (colorectal) cancer DNA hypomethylation is thought to be the link between the observed relationship between inadequate folate status and cancer. There are many factors that contribute to the fact that the status of these vitamins in the elderly is inadequate. These factors are in part physiological such as the achlorhydria which affects vitamin B12 absorption and in part socioeconomic and habitual. We need more studies to confirm that these vitamins have important functions in the etiology of these diseases. We also need to establish if these diseases can be prevented or diminished by proper nutrition starting at a younger age.
Chemoprevention of bladder cancer.

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Abstract

The data presented herein, although highly supportive for a protective role of various nutrients against bladder cancer, are far from definitive. Many authorities question the validity of current recommendations for nutritional chemoprevention against bladder cancer. The reason for the wide variations reported in epidemiologic studies lies in the nature of observational studies. Dietary studies are limited in their conclusions because the protection afforded by the consumption of a particular nutrient may be multifactorial, with different components of the food exerting potential chemopreventive effects. Furthermore, measuring levels of nutrients in the food intake of populations is confounded by factors that might affect these levels and also the incidence of cancer. For example, vitamin A can come from animal or vegetarian sources. Because animal fat has been identified as a potential carcinogen in man, depending on the source of the vitamin, varying levels of protection might be deduced. In addition, chemoprevention studies using dietary supplements are expected to have mild effects, and large studies would be required to confirm statistical significance. Even with agents such as intravesical chemotherapy, only half the studies achieve statistical significance [29]. Prospective randomized trials with a large sample size, longer follow-up, and an extended duration of treatment are needed to clarify the association between micronutrients and cancer protection. With these caveats in mind, several recommendations can be made. Simple measures, such as drinking more fluids (especially water), can have a profound impact on the incidence of bladder cancer. Vitamins are being extensively studied in chemopreventive trials for different cancers. There is strong evidence for a chemoprotective effect of vitamin A in bladder cancer. The authors recommend 32,000 IU/day of vitamin A initially, with lower doses (24,000 IU) for persons less than 50 kg. Because liver toxicity is a possibility with long-term administration, the dose should be decreased to 16,000 IU after 3 years. High doses of beta-carotene should be avoided based on a large clinical trial reporting a 25% increase in the number of cases of prostate cancer and a statistically significant increase in the incidence of lung cancer. Vitamin B6 has been studied in several clinical trials in bladder cancer. The US-based Veterans Administration cooperative study found benefit for vitamin B6 when given as a single agent. Data for vitamins C and E are insufficient to recommend either agent as stand-alone treatment. Nonetheless, each of these vitamins is known to have beneficial effects, including improved function of the immune system. It is possible that only a small percentage of patients with bladder cancer respond to vitamins B6, C, or E, yet each is safe, nontoxic, and inexpensive. In an effort to pool the efficacy of individual agents and to increase the power of study, the authors evaluated the combination of vitamins A, B6, C, and E in a double-blind trial. The observed 50% 5-year reduction in tumor recurrence was highly significant and greater than would be expected for any of the individual ingredients and suggests that combinations of nutritional agents may be most appropriate. A large-volume study along similar lines is being conducted. Among the numerous other compounds and dietary substances purported to have chemopreventive effect, soybeans, garlic, and green tea stand out as having the greatest promise and can freely be recommended to patients. For synthetically synthesized agents such as celecoxib, piroxicam, or DFMO, recommendations must be deferred until the results of clinical trials are conclusively in favor of their use. Many of the dietary factors found to be protective against bladder cancer are being investigated in other cancers and are beneficial to general health.
Although naturally occurring nutrients are ideal, especially because the delicate balance of various micronutrients might be impossible to synthesize in the laboratory, the general population finds it easier to take vitamin supplements. Unfortunately, dietary changes such as decreasing fat and increasing fruit and vegetable intake are more difficult to initiate. There is a mistaken notion that simply because an agent is naturally occurring, it cannot be as beneficial as taking a substance synthesized in the laboratory. Even in a high-risk group such as nuclear-bomb survivors in Japan, high consumption of vegetables and fruit is protective against bladder cancer [44]. Encouraging patients to follow an essentially healthy food habit lifestyle will be a significant contribution in the fight against cancer.

PMID: 12109342 [PubMed - indexed for MEDLINE]
Chemoprevention of urological cancer.

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Abstract

PURPOSE: Cancer is a major cause of mortality and morbidity throughout the world, and ranks as the second leading cause of death in the United States. Most cancers have a latent period of 10 to 20 years, which provides ample time for preventive measures. Transitional cell carcinoma of the bladder and adenocarcinoma of the prostate have protracted courses and may be ideal for chemopreventive strategies. We review the biochemistry and epidemiology of chemopreventive agents, and the laboratory and clinical studies of their role in urological cancer.

MATERIALS AND METHODS: We performed a computerized MEDLINE search and manual bibliographical review of relevant peer reviewed studies and reports from 1966 to 1998. These reports were analyzed and scrutinized, and the important findings are summarized.

RESULTS: Neoplastic lesions of the bladder and prostate are uniquely suited to the development and evaluation of chemopreventive agents. Epidemiological reports provide the strongest evidence of a protective role for dietary agents in cancer of the bladder, prostate and kidney. Observational and recent experimental trials support these findings in cases of adenocarcinoma of the prostate and transitional cell carcinoma of the bladder. There is strong evidence for a protective effect of vitamin A in bladder cancer. Superior protection has been reported with a combination of high doses of vitamins A, B6, C and E plus zinc. For prostate cancer strong evidence exists for a preventive effect of reduced fat intake, vitamin E, selenium and soy proteins. A lesser benefit is also suggested with intake of vitamins D and C. Evidence of chemoprevention against renal cell cancer is supported mainly by epidemiological studies, and animal studies indicate possible benefit of vitamin D supplementation.

CONCLUSIONS: Although there is no incontrovertible proof, numerous studies implicate dietary and nutritional factors in the onset and progression of cancer of the bladder, prostate and kidney. It is possible that the preventive effect of dietary constituents may be in part from consumption with other nutrients and bioactive compounds in whole foods. Further research is needed before vitamins and other nutritional supplements can be advocated as standard therapy but the preponderance of evidence supports increased intake of vitamins A, B6, C, D and E, reduction of animal fat, and increased consumption of fruits and vegetables.

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Periconceptional multivitamin administration result in reduction of congenital abnormalities: adequate evidence for formulating national recommendations for Germany?

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Abstract
In the discussion about primary prevention of congenital abnormalities, vitamins often have been picked out as a central theme in literature. In randomised controlled trials, a significant reduction of congenital abnormalities up to 17% by the periconceptional use of multivitamins (folic acid, vitamin B12, vitamin B6, vitamin C and zinc) were found. This protective effect can be explained by lower prevalence of neural tube defects, cardiovascular malformations, malformations of the urinary system, limb deficiencies and hypertrophic pyloric stenosis. Multivitamin consumption including 0.8 mg folic acid for at least 28 days before conception and continuing for at least until the second missed menstrual period, have been most effective. These findings in primary prevention of congenital abnormalities raise an import public health issue. Therefore, for women of childbearing age, there are three possibilities of primary prevention of congenital abnormalities: 1. consumption of a vitamin-rich diet, 2. supplementation of vitamins, and 3. food fortification with vitamins. With regard to an appropriate consumption of multivitamins in practice, there are many problems. To ensure that in Germany all women of childbearing age will benefit from the discussions and findings of other countries, food fortification with folic acid and other vitamins should be checked. Furthermore, implementation of a national health policy for Germany should be considered.

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Primary oxalosis: clinical and biochemical response to high-dose pyridoxine therapy.
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Abstract
Although pyridoxine hydrochloride (vitamin B6) is known to reduce the endogenous production of oxalate in some individuals with primary oxalosis, the dose for a satisfactory trial of treatment is not established. We report two cases of primary oxalosis on a daily regimen of 1 g pyridoxine hydrochloride, in which 24-hr urinary oxalate excretion decreased by 60% and 70%, respectively, with corresponding clinical benefit. The responses have been sustained up to 2.5 yr in one case, and 20 mo in the other. In the patient with renal failure, serum creatinine decreased from 243 to 146 mumole/liter after 15 mo of treatment. The decrease in glycolic acid excretion in both patients was consistent with an increase of glyoxalate transaminase activity by the vitamin. Supranormal levels of erythrocyte glutamic oxaloacetate transaminase (egot) activity were observed during therapy, and these may be useful as a measure of the effective dose of pyridoxine.

PMID: 449695 [PubMed - indexed for MEDLINE]