

DIALIX R - Published Research Abstracts

Omega-3: EPA y DHA

[Am J Kidney Dis.](#) 2010 May 19. [Epub ahead of print]

Omega-3 Polyunsaturated Fatty Acids in the Treatment of Kidney Disease.

[Fassett RG](#), [Gobe GC](#), [Peake JM](#), [Coombes JS](#).

Renal Research, Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia; University of Queensland, School of Human Movement Studies, Brisbane, Queensland, Australia; University of Queensland, Centre for Kidney Disease Research, School of Medicine, Brisbane, Queensland, Australia.

Abstract

After more than 25 years of published investigation, including randomized controlled trials, the role of omega-3 polyunsaturated fatty acids in the treatment of kidney disease remains unclear. In vitro and in vivo experimental studies support the efficacy of omega-3 polyunsaturated fatty acids on inflammatory pathways involved with the progression of kidney disease. Clinical investigations have focused predominantly on immunoglobulin A (IgA) nephropathy. More recently, lupus nephritis, polycystic kidney disease, and other glomerular diseases have been investigated. Clinical trials have shown conflicting results for the efficacy of omega-3 polyunsaturated fatty acids in IgA nephropathy, which may relate to varying doses, proportions of eicosapentaenoic acid and docosahexaenoic acid, duration of therapy, and sample size of the study populations. Meta-analyses of clinical trials using omega-3 polyunsaturated fatty acids in IgA nephropathy have been limited by the quality of available studies. However, guidelines suggest that omega-3 polyunsaturated fatty acids should be considered in progressive IgA nephropathy. Omega-3 polyunsaturated fatty acids decrease blood pressure, a known accelerant of kidney disease progression. Well-designed, adequately powered, randomized, controlled clinical trials are required to further investigate the potential benefits of omega-3 polyunsaturated fatty acids on the progression of kidney disease and patient survival.

PMID: 20493605 [PubMed - as supplied by publisher]

[J Ren Nutr.](#) 2010 Sep;20(5):321-8. Epub 2010 Mar 19.

Effects of omega-3 polyunsaturated fatty-acid supplementation on redox status in chronic renal failure patients with dyslipidemia.

[Bouzidi N](#), [Mekki K](#), [Boukaddoum A](#), [Dida N](#), [Kaddous A](#), [Bouchenak M](#).

Laboratoire de Nutrition Clinique et Métabolique, Département de Biologie, Faculté des Sciences, Université d'Oran, Es-Sénia, Oran, Algeria.

Abstract

OBJECTIVE: We sought to evaluate the effects of omega-3 polyunsaturated fatty-acid (PUFA) supplementation on dyslipidemia, lipid and protein peroxidation, and antioxidant defense in patients with chronic renal failure (CRF).

DESIGN: Eighty patients with CRF were diagnosed in the hospital of Oran between January 2008 and April 2008. Forty patients (male/female, 22/18; aged 61 +/- 14 years, S.D.) were available for the study. They presented with dyslipidemia and hypertriglyceridemia (triacylglycerols, >1.7 mmol/L) and/or hypercholesterolemia (total cholesterol, >5 mmol/L).

INTERVENTION: All patients received nutritional counsel adapted to CRF, i.e., energy intake of .12 megajoule x kg(-1) x body weight x day(-1), protein intake of .8 g x kg(-1) x body weight x day(-1), and lipid intake of 35% of total energy intake with 28% PUFAs, 37% monounsaturated fatty acids, and 35% saturated fatty acids. Patients were randomized into two groups: 20 received supplementation with omega-3 fish oil (2.1 g . day(-1)) for 90 days, and 20 were used as controls. To control the counsel monitoring, a nutritional survey was performed at baseline and at 12 weeks. Blood samples were drawn at the beginning (T0), at 30 days (T1), at 60 days (T2), and at 90 days (T3) after initiating treatment.

RESULTS: In the omega-3 group, a reduction in triacylglycerol levels was evident at T1 (-43%), T2, and T3 (-48%). Thiobarbituric acid-reactive substances were at lower levels at T1 and T3. There was no significant difference in carbonyl values, whereas serum superoxide dismutase and glutathione peroxidase activities were increased at T1, T2, and T3. High catalase activity was evident at T2 and T3.

CONCLUSION: Omega-3 supplementation improves hypertriglyceridemia and oxidative stress in patients with CRF, and may lead to decreased rates of cardiovascular complications.

PMID: 20303788 [PubMed - in process]

[J Biol Chem](#). 2010 Aug 23. [Epub ahead of print]

ARACHIDONIC ACID-METABOLIZING CYTOCHROME P450 ENZYMES ARE TARGETS OF OMEGA-3 FATTY ACIDS.

[Arnold C](#), [Markovic M](#), [Blossey K](#), [Wallukat G](#), [Fischer R](#), [Dechend R](#), [Konkel A](#), [von Schacky C](#), [Luft FC](#), [Muller DN](#), [Rothe M](#), [Schunck WH](#).

Max Delbrueck Center for Molecular Medicine, Germany;

Abstract

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) protect against cardiovascular disease by largely unknown mechanisms. We tested the hypothesis that EPA and DHA may compete with arachidonic acid (AA) for the conversion by cytochrome P450 (CYP) enzymes resulting in the formation of alternative, physiologically active, metabolites. Renal and hepatic microsomes, as well as various CYP-isoforms, displayed equal or elevated activities when metabolizing EPA or DHA instead of AA. CYP2C/2J-isoforms converting AA to epoxyeicosatrienoic acids (EETs) preferentially epoxidized the omega-3 double bond and thereby produced 17,18-epoxyeicosatetraenoic (17,18-EEQ) and 19,20-epoxydocosapentaenoic acid (19,20-EDP) from EPA and DHA. We found that these omega-3 epoxides are highly active as antiarrhythmic agents, suppressing Ca²⁺-induced increased rate of spontaneous beating of neonatal rat cardiomyocytes, at low nanomolar concentrations. CYP4A/4F-isoforms omega-hydroxylating AA were less regioselective towards EPA and DHA, catalyzing predominantly omega- and omega minus-1 hydroxylation. Rats given dietary EPA/DHA supplementation exhibited substantial replacement of AA by EPA and DHA in membrane phospholipids in plasma, heart, kidney, liver, lung, and pancreas, with less pronounced changes in brain. The changes in fatty acids were accompanied by concomitant changes in endogenous CYP metabolite profiles (e.g. altering the EET:EEQ:EDP ratio from 87:0:13 to 27:18:55 in the heart). These results demonstrate that CYP-enzymes efficiently convert EPA and DHA to novel epoxy- and hydroxy-metabolites that could mediate some of the beneficial cardiovascular effects of dietary omega-3 fatty acids.

PMID: 20732876 [PubMed - as supplied by publisher]

[Prostaglandins Leukot Essent Fatty Acids](#). 2010 Jan;82(1):35-44. Epub 2009 Nov 20.

Studies on the protective effect of dietary fish oil on uranyl-nitrate-induced nephrotoxicity and oxidative damage in rat kidney.

[Priyamvada S](#), [Khan SA](#), [Khan MW](#), [Khan S](#), [Farooq N](#), [Khan F](#), [Yusufi AN](#).

Department of Biochemistry, Faculty of Life Sciences, Aligarh Muslim University, Aligarh 202002, UP, India.

Abstract

Human and animal exposure demonstrates that uranium is nephrotoxic. However, attempts to reduce it were not found suitable for clinical use. Dietary fish oil (FO) enriched in omega-3 fatty acids reduces the severity of cardiovascular and renal diseases. Present study investigates the protective effect of FO on uranyl nitrate (UN)-induced renal damage. Rats prefed with experimental diets for 15 days, given single nephrotoxic dose of UN (0.5mg/kg body weight) intraperitoneally. After 5d of UN treatment, serum/urine parameters, enzymes of carbohydrate metabolism, brush border membrane (BBM), oxidative stress and phosphate transport were analyzed in rat kidney. UN nephrotoxicity was characterized by increased serum creatinine and blood urea nitrogen. UN increased the activity of lactate dehydrogenase and NADP-malic enzyme whereas decreased malate, isocitrate and glucose-6-phosphate dehydrogenases; glucose-6-phosphatase, fructose-1, 6-bisphosphatase and BBM enzyme activities. UN caused oxidant/antioxidant imbalances as reflected by increased lipid peroxidation, activities of superoxide dismutase, glutathione peroxidase and decreased catalase activity. Feeding FO alone increased activities of enzymes of glucose metabolism, BBM, oxidative stress and Pi transport. UN-elicited alterations were prevented by FO feeding. However, corn oil had no such effects and was not similarly effective. In conclusion, FO appears to protect against UN-induced nephrotoxicity by improving energy metabolism and antioxidant defense mechanism.

PMID: 19931439 [PubMed - indexed for MEDLINE]

[Curr Pharm Des.](#) 2009;15(36):4149-56.

Omega-3 and renal function in older adults.

[Lauretani F](#), [Maggio M](#), [Pizzarelli F](#), [Michelassi S](#), [Ruggiero C](#), [Ceda GP](#), [Bandinelli S](#), [Ferrucci L](#).

Geriatric Unit, Geriatric-Rehabilitation Department, University Hospital of Parma, Parma, Italy.

flauretani@ao.pr.it

Abstract

Chronic kidney disease (CKD) is a major public health problem and can result in end-stage renal disease with need for dialysis or transplantation. In Europe up to 12% of the adult population had some renal impairment, while in the United States the end stage of CKD has increased dramatically from 209.000 in 1991 to 472.000 in 2004. Diabetes and hypertension are major causes of kidney pathology. Infection, particularly ascending infection, is more common with increasing age, as both immune function declines and associated pathology predisposing to infection, such as obstructive uropathy, becomes more common. Most pathological changes in the kidney appear to be initiated by oxidative stress, followed by an inflammatory reaction. Oxidative stress results from an imbalance between free radicals and their detoxification by endogenous and exogenous scavengers, including polyunsaturated fatty acids (PUFA). Recent studies showed that PUFA supplementation slowed the rate of loss of renal function in patients with IgA nephropathy. Then, studies of omega-3 supplementation in dialysis patients describe salutary effects on triglyceride levels and dialysis access patency. We examined the relationship between total plasma PUFA levels and change in creatinine clearance over a three-year follow-up in the older persons enrolled in the InCHIANTI study, a population-based epidemiology study conducted in Tuscany, Italy. This study showed that older adults with low total plasma PUFA levels have a greater decline in creatinine clearance over three years of follow-up. These findings suggest that a higher dietary intake of PUFA may be protective against progression to chronic kidney disease.

PMID: 20041816 [PubMed - indexed for MEDLINE]PMCID: PMC2863302Free

[J Immunol.](#) 2009 Mar 1;182(5):3223-32.

Acute changes in dietary omega-3 and omega-6 polyunsaturated fatty acids have a pronounced impact on survival following ischemic renal injury and formation of renoprotective docosahexaenoic acid-derived protectin D1.

[Hassan IR](#), [Gronert K](#).

New York Medical College, Department of Pharmacology, Valhalla, NY 10595, USA.

Abstract

Exacerbated inflammation plays an important role in the pathogenesis of ischemic renal injury (IRI), which is the major cause of intrinsic acute renal failure. Clinical studies suggest that long-term treatment with omega-3 polyunsaturated fatty acids (PUFA) improves renal function and lowers the risk of death or end-stage renal disease. Docosahexaenoic acid, a principle omega-3 PUFA of fish oils, is of particular interest as it is found in most human tissues and is converted to protectin D1 (PD1), which exhibits antiinflammatory and proresolving bioactions. We set out to investigate the impact of acute dietary modulation of omega-3 or omega-6 PUFA on IRI and renal lipid autacoid circuits, using an established mouse model and liquid chromatography-mass spectroscopy/mass spectroscopy-based lipidomics. Thirty minutes of renal ischemia significantly elevated serum creatinine in the omega-6 diet group while renal function remained normal in the matched omega-3 diet group. Notably, extending ischemia to 45 min caused 100% mortality in the omega-6 group, in sharp contrast to 0% mortality in the omega-3 group. Protection against IRI in the omega-3 group correlated with decreased polymorphonuclear leukocyte recruitment, chemokine and cytokine levels, abrogated formation of lipoxygenase- and cyclooxygenase-derived eicosanoids, and increased renal levels of PD1. Systemic treatment with PD1 reduced kidney polymorphonuclear leukocyte influx and, more importantly, amplified renoprotective heme-oxygenase-1 protein and mRNA expression in injured and uninjured kidneys. These findings suggest therapeutic or dietary amplification of PD1 circuits restrains acute renal injury and that short-term changes in dietary omega-3 and omega-6 PUFA dramatically impacts renal lipid autacoid formation and outcome of IRI.

PMID: 19234220 [PubMed - indexed for MEDLINE]

[Am J Physiol Renal Physiol](#). 2009 Feb;296(2):F306-16. Epub 2008 Dec 3.

Omega-3 fatty acid rich diet prevents diabetic renal disease.

[Garman JH](#), [Mulrone S](#), [Manigrasso M](#), [Flynn E](#), [Maric C](#).

Dept. of Physiology and Biophysics, Univ. of Mississippi Medical Center, 2500 North State St., Jackson, MS 39216, USA.

Abstract

Omega-3 polyunsaturated fatty acids (n-3 PUFA) show beneficial effects in cardiovascular disease, IgA, and diabetic nephropathy; however, the mechanisms underlying these benefits are unknown. The study was performed in male Sprague-Dawley rats randomly divided into four treatment groups: nondiabetic (ND), streptozotocin-induced diabetic (D), diabetic and fed a high n-3 PUFA diet (D+canola), and diabetic and fed a high n-6 (omega-6) PUFA diet (D+corn). Study treatments were carried out for 30 wk. D+canola significantly decreased diabetes-associated increases in urine albumin excretion (ND 17.8 +/- 6.4; D 97.3 +/- 9.4; D+canola 8.3 +/- 2.2 mg/day); systolic blood pressure (ND 153 +/- 9; D 198 +/- 7; D+canola 162 +/- 9 mmHg); glomerulosclerosis (ND 0.6 +/- 0.2; D 1.8 +/- 0.2; D+canola 0.8 +/- 0.1 AU); and tubulointerstitial fibrosis in the renal cortex (ND 1.2 +/- 0.2; D 2.0 +/- 0.2; D+canola 1.1 +/- 0.1) and the inner stripe of the outer medulla (ND 1.0 +/- 0.2; D 2.1 +/- 0.2; D+canola 1.1 +/- 0.2 AU). D+corn also exerted renoprotection, but not to the same degree as D+canola (urine albumin excretion, 33.8 +/- 6.1 mg/day; systolic blood pressure, D+corn 177 +/- 6 mmHg; glomerulosclerosis, D+corn 1.2 +/- 0.3 AU; cortical tubulointerstitial fibrosis, D+corn 1.6 +/- 0.1 AU; medullary tubulointerstitial fibrosis, D+corn 1.5 +/- 0.1 AU). In addition, D+canola attenuated D-associated increase in collagen type I and type IV, IL-6, MCP-1, transforming growth factor-beta, and CD68 expression. These observations indicate a beneficial effect of high dietary intake of n-3 PUFA in reducing diabetic renal disease.

PMID: 19052104 [PubMed - indexed for MEDLINE]

Rehmannia glutinosa

[J Ethnopharmacol](#). 2009 Feb 25;122(1):131-5. Epub 2008 Dec 25.

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

[Lee BC](#), [Choi JB](#), [Cho HJ](#), [Kim YS](#).

Department of Internal Medicine, College of Oriental Medicine, Kyung Hee University, 1 Hoegi-dong, Dongdaemun-Ku, Seoul 130-702, Republic of Korea.

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.

[J Ethnopharmacol](#). 2008 Aug 13;118(3):466-72. Epub 2008 May 23.

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.

[Liu HR](#), [Tang XY](#), [Dai DZ](#), [Dai Y](#).

Research Division of Pharmacology, China Pharmaceutical University, Nanjing, China.

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 metalloproteinases) 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.

[Biol Pharm Bull.](#) 2005 Sep;28(9):1662-7.

Rehmannia glutinose ameliorates renal function in the ischemia/reperfusion-induced acute renal failure rats.

[Kang DG](#), [Sohn EJ](#), [Moon MK](#), [Lee YM](#), [Lee HS](#).

Professional Graduate School of Oriental Medicine and Medicinal Resources Research Institute (MeRRI), Wonkwang University, Jeonbuk, Republic of Korea.

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]

[Zhongguo Zhong Xi Yi Jie He Za Zhi](#). 2004 Dec;24(12):1084-6.

Clinical study on treatment of mid-advanced crescentic nephritis by qingre huoxue recipe

[Article in Chinese]

[Deng YY](#), [Chen YP](#), [Wang L](#), [Hu Z](#), [Jin Y](#), [Shen L](#), [Zhu R](#), [Zhong Y](#).

Department of Nephrology, Longhua Hospital, Shanghai University of TCM, Shanghai 200032.

yueyideng@hotmail.com

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.

[Am J Chin Med.](#) 2004;32(6):829-39.

Amelioration of diabetic nephropathy by dried *Rehmanniae Radix* (Di Huang) extract.

[Yokozawa T](#), [Kim HY](#), [Yamabe N](#).

Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, Toyama 930-0194, Japan.
yokozawa@ms.toyama-mpu.ac.jp

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]

[Zhongguo Zhong Xi Yi Jie He Za Zhi](#). 1993 May;13(5):269-72, 259-60.

Clinical and experimental study on effects of man-shen-ling oral liquid in the treatment of 100 cases of chronic nephritis

[Article in Chinese]

[Su ZZ](#), [He YY](#), [Chen G](#).

Worker's Hospital of the 5th Metallurgical Construction Company, Chengdu.

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]

Astragalus membranaceus

[Urol Res.](#) 2010 Jul 6. [Epub ahead of print]

The protective effects of the traditional Chinese herbs against renal damage induced by extracorporeal shock wave lithotripsy: a clinical study.

[Sheng B](#), [He D](#), [Zhao J](#), [Chen X](#), [Nan X](#).

Department of Geriatric Surgery, The Afflicted First Hospital, School of Medicine, Xi'an Jiaotong University, Xi'an, 710061, Shaanxi, China.

Abstract

Extracorporeal shock wave lithotripsy (ESWL)-induced renal damage can occur as a result of multiple mechanisms. We have reported previously that *Astragalus membranaceus*, *Salvia miltiorrhiza*, a decoction of six drugs containing rhizoma *Rehmanniae preparata* and supplements of a few traditional Chinese medicinal herbs for invigorating the kidney and excreting calculus, have a protective effect on renal injury induced by high-energy shock waves (HESW) in rabbits. In this clinical study we further investigate the protective effects of these traditional Chinese herbs against renal damage induced by ESWL. Sixty consenting patients with renal calculus who underwent ESWL treatment were included and randomly assigned to the medication group or control group. Post-ESWL plasma nitric oxide (NO), endothelin-1 (ET-1), malondialdehyde (MDA), and serum tumor necrosis factor alpha (TNF-alpha) increased significantly in the controls ($P < 0.05$), while in the medication group, slightly but not significantly elevated levels of plasma ET-1, NO, and serum TNF-alpha were found. The difference between the groups was statistically significant ($P < 0.05$). The levels of superoxide dismutase (SOD) decreased gradually in the controls, reaching a trough 72 h after ESWL ($P < 0.05$), while in the treated group it was unchanged, and remained at a level higher versus the controls ($P < 0.05$). Plasma NO peaked twice by 72 h and at 1 week in the controls ($P < 0.05$). Urinary enzymes and beta(2)-microglobulin increased significantly and peaked by 24 h and immediately after ESWL ($P < 0.05$). These values were greater in the controls, and the difference was statistically significant ($P < 0.05$). This study demonstrates that the preparations of traditional Chinese medicines for invigorating the kidney and excreting calculus can reduce renal tubular damage induced by ESWL, and can shorten the recovery time of renal tubules in human subjects.

PMID: 20607528 [PubMed - as supplied by publisher]

[Phytother Res.](#) 2010 Jun;24(6):875-84.

Effect of Astragalus membranaceus and Angelica sinensis combined with Enalapril in rats with obstructive uropathy.

[Wojcikowski K](#), [Wohlmuth H](#), [Johnson DW](#), [Gobe G](#).

Molecular and Cellular Pathology, School of Medicine, University of Queensland, Brisbane, Queensland, Australia. kwojciko@scu.edu.au

Abstract

ACE inhibitors (ACEi) reduce renal tubulointerstitial fibrosis but are not completely effective. Combined extract of *Astragalus membranaceus* and *Angelica sinensis* (A&A) is a traditional antifibrotic agent in China. The present investigation aimed to determine whether an ACEi (Enalapril) and A&A together have a better antifibrotic effect in unilateral ureteral obstruction (UUO) than monotherapy with either agent. Male Sprague-Dawley rats (N = 4 per group) had either sham operation or UUO alone, with A&A (combined aqueous and ethanol extract equivalent to 2.1 g dried herbs), with Enalapril (in drinking water at 200 mg/mL) or with both treatments. Kidney and liver were collected for protein extraction or fixed for histologic stains, immunohistochemistry (IHC), microscopy. Enalapril or A&A individually were antifibrotic. Transforming growth factor-beta1, fibroblast activation, collagen deposition, macrophage accumulation and tubular cell apoptosis were all decreased. The combination of the two drugs was significantly more effective than Enalapril alone in reducing tumor necrosis factor-alpha, collagen accumulation, activation of fibroblasts, and tubular cell apoptosis. In conclusion, Enalapril with A&A significantly decreased tubulointerstitial fibrosis to a greater extent than treatment with Enalapril alone. Further studies focusing on the isolation of the active constituents of A&A and the clinical application of the combination of ACEi plus A&A are warranted to determine the value of this treatment in humans.

PMID: 19960445 [PubMed - indexed for MEDLINE]

[Vascu Pharmacol.](#) 2009 May-Jun;50(5-6):185-93.

A combination of Chinese herbs, *Astragalus membranaceus* var. *mongholicus* and *Angelica sinensis*, improved renal microvascular insufficiency in 5/6 nephrectomized rats.

[Song J](#), [Meng L](#), [Li S](#), [Qu L](#), [Li X](#).

Renal Division, Department of Medicine, Peking University First Hospital, Beijing 100034, PR China.

Abstract

Chronic renal ischemia and hypoxia in the tubulointerstitium are involved in the mechanisms of progressive chronic kidney disease. Previous studies showed that the decoction of a combination of two Chinese herbs, *Astragalus membranaceus* var. *mongholicus* and *Angelica sinensis* (A & A) has antifibrotic effects through multiple pathways in different animal models. In this study, remnant kidney model was employed to investigate whether A & A affect the expression of VEGF, the density of the renal microvasculature and thus alleviate the renal injury. Rats were divided randomly into four groups: sham group (N=31), 5/6 Nx group (5/6 nephrectomy, N=43), A & A treated group (A & A group, N=40, A & A 12 g/kg/d po), enalapril treated group (Ena group, N=56, enalapril 4 mg/kg/d po). Rats from each group were sacrificed at the 2th, 4th, 8th and 12th weeks respectively after surgery and treatment. The 24 h urinary protein excretion, serum creatinine (Scr) and urea were measured. The collagen IV (COL-IV), fibronectin (FN), aminopeptidase P (APP) and VEGF were stained using immunohistochemistry. The COL-IV, FN and APP were semi-quantitatively analyzed. Peritubular capillary density in the cortical interstitial area was quantified. The level of VEGF was assayed by ELISA. The results revealed that Scr, urea and urinary protein excretion remained constant at each time point in sham group. Compared to sham group, 5/6 Nx group was shown severe glomerulosclerosis, tubulointerstitial lesions and vascular damage, as well as higher level of Scr from the 2nd week (72.3 +/- 5.2 vs. 48.6 +/- 2.6 micromol/L P < 0.05) to the 12th week (71.9 +/- 8.0 vs. 55.7 +/- 4.5 micromol/L P < 0.05). Although there was no significant difference in Scr level after treatment of enalapril or A & A (P > 0.05), kidney damage was alleviated at the 8th and the 12th week in the two treatment groups (P < 0.05, vs. 5/6 Nx group). The urinary protein excretion of 5/6 Nx group was significantly increased from the 4th week, it was 1.5, 2.4 and 3.8 fold of that of sham group at the 4th, 8th and 12th week, respectively. Compared to 5/6 Nx group, proteinuria was decreased by enalapril to 59%, 33% at 8th and 12th week. After A & A administration, urinary protein excretion decreased to 66%, 56%, 75%, 55% of 5/6 Nx group at the 2nd, 4th, 8th and 12th, respectively (P < 0.05). Compared with sham group, there was increased expression of FN and COL-IV in rats with 5/6 Nx. After A & A or enalapril administration, the expression of FN and COL-IV was significantly decreased compared with that in the 5/6 Nx group at 8th and 12th week (P < 0.05). On the other hand, the capillary density was decreased at the 8th and 12th week in 5/6 Nx rats (P < 0.01). In A & A-treated group, similarly with enalapril group, the amount of APP-positive glomerular capillary increased by 36% (P < 0.01), and the peritubular capillary density was increased 94% at 8th week and 52% at 12th week compared with 5/6 Nx group (P < 0.05). The renal level of VEGF was decreased in 5/6 Nx rats, but increased at the 8th and 12th week in A & A group (P < 0.05, vs. 5/6 Nx group). In conclusion, A & A has renoprotective effects by suppression of extra cellular matrix deposition in 5/6 Nx rat. The renoprotective effects may be associated with reduction of proteinuria, up-regulation of VEGF which may reduce the loss of capillaries and improve microstructure dysfunction.

PMID: 19563735 [PubMed - indexed for MEDLINE]

[J Ethnopharmacol](#). 2009 Nov 12;126(2):189-96. Epub 2009 Sep 6.

Systematic review of the renal protective effect of *Astragalus membranaceus* (root) on diabetic nephropathy in animal models.

[Zhang J](#), [Xie X](#), [Li C](#), [Fu P](#).

Department of Nephrology, West China Hospital of Sichuan University, Chengdu 610041, China.

Abstract

GOALS: Diabetic nephropathy (DN) has long been recognized as the leading cause of end-stage renal disease. Recent experimental studies have shown that *Astragalus membranaceus* (AM) (root) has an inhibitory effect on the oxidative stress that characterizes early DN. This systematic review assesses the efficacy and safety of AM (root), used as a single herb, in slowing the progression of DN in diabetic rat models.

METHODS: We conducted both an electronic search and a search by hand of randomized, controlled AM (root) treatment studies (including its effective components) focusing on animal models of DN. Two reviewers independently selected and assessed the studies.

RESULTS: Among the 41 articles identified, 13 reports that fulfilled the inclusion criteria were included. Significant beneficial effects were observed in the AM (root) treated groups compared to controls regarding fasting blood glucose levels (standardized mean difference [SMD]: -2.86, 95% confidential interval (CI): -4.26, -1.46, $P < 0.001$), glomerular filtration rate (SMD: -3.36, 95% CI: -4.69, -2.03, $P < 0.00001$), urinary albumin excretion rate (SMD: -2.46, 95% CI: -3.75, -1.16, $P = 0.0002$), and thickness of the glomerular basement membrane (SMD: -3.51, 95% CI: -6.68, -0.34, $P = 0.03$).

CONCLUSIONS: AM (root) and its effective components are effective in reducing fasting blood glucose and albuminuria levels, in reversing the glomerular hyperfiltration state, and in ameliorating the pathological changes of early DN in rat models.

PMID: 19735713 [PubMed - indexed for MEDLINE]

[Am J Kidney Dis.](#) 2007 Dec;50(6):1028-32.

Treatment of idiopathic membranous nephropathy with the herb *Astragalus membranaceus*.

[Ahmed MS](#), [Hou SH](#), [Battaglia MC](#), [Picken MM](#), [Leehey DJ](#).

Department of Medicine, Loyola University Medical Center, Maywood, IL 60153, USA.

Comment in: [Am J Kidney Dis.](#) 2010 Apr;55(4):772.

Abstract

A 77-year-old woman with nephrotic syndrome secondary to idiopathic membranous nephropathy was treated with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, cyclosporine A, and mycophenolate mofetil, without response. After more than 2 years of unremitting nephrosis, she began therapy with the herb *Astragalus membranaceus*, used by traditional Chinese physicians to treat various immune disorders, including glomerulonephritis. After institution of *Astragalus* at a dose of 15 g/d, there was a marked decrease in proteinuria. Nephrotic syndrome recurred after temporary cessation of *Astragalus* therapy, with complete remission of nephrosis observed after its reintroduction. The clinical course of this patient suggests that *Astragalus* may have beneficial effects in patients with idiopathic membranous nephropathy.

PMID: 18037104 [PubMed - indexed for MEDLINE]

Cordyceps sinensis

[Fitoterapia](#). 2010 Jul;81(5):397-402. Epub 2009 Dec 4.

Protection of chronic renal failure by a polysaccharide from Cordyceps sinensis.

[Wang Y](#), [Yin H](#), [Lv X](#), [Wang Y](#), [Gao H](#), [Wang M](#).

School of Life Science and Technology, China Pharmaceutical University, Nanjing, Jiangsu, People's Republic of China.

Abstract

A water-soluble polysaccharide (CPS-2), isolated from the cultured *Cordyceps sinensis*, was obtained by hot-water extraction, anion-exchange and gel permeation chromatography. Its structural characteristics were investigated by PMP pre-column derivation, periodate oxidation, methylation analysis, FTIR and NMR spectroscopy. CPS-2 was found to be mostly of alpha-(1-->4)-D-glucose and alpha-(1-->3)-D-mannose, branched with alpha-(1-->4,6)-D-glucose every twelve residues on average. CPS-2 had a molecular weight of 4.39×10^4 Da. The protective effect of CPS-2 on the model of chronic renal failure was established by fulgerizing kidney. The changes in blood urea nitrogen and serum creatinine revealed that CPS-2 could significantly relieve renal failure caused by fulgerizing kidney.

PMID: 19969045 [PubMed - in process]

[Am J Chin Med.](#) 2009;37(5):977-89.

Structural determination and antioxidant activity of a polysaccharide from the fruiting bodies of cultured *Cordyceps sinensis*.

[Wang Y](#), [Wang M](#), [Ling Y](#), [Fan W](#), [Wang Y](#), [Yin H](#).

Department of Microbiology and Biochemistry, School of Life Science and Technology, China Pharmaceutical University, Jiangsu, China. wangying19830511@hotmail.com

Abstract

A water-soluble polysaccharide named CPS1 had been isolated from *C. sinensis* mycelium by hot water extraction, ethanol precipitation, anion-exchange, and gel-permeation chromatography. UV spectra, FTIR spectra, partial acid hydrolysis, PMP precolumn derivation, periodate oxidation and Smith degradation studies were conducted to elucidate its structure. The results indicated that CPS1 was a glucomannogalactan with the monosaccharide composition of glucose: mannose: galactose = 2.8: 2.9: 1. The total carbohydrate content of CPS1 was 99.0%. The weight-average molecular weight was 8.1×10^3 Da. The results predicted (1 \rightarrow 2) and (1 \rightarrow 4)-linkage of mannose, (1 \rightarrow 3)-linkage of galactose, (1 \rightarrow) and (1 \rightarrow 3, 6)-linkage of glucose composed the backbone of CPS1. CPS1 was also evaluated for its antioxidant activity in vitro, including scavenging effects on the hydroxyl radicals, the reducing power, Fe(2+)-chelating activity, scavenging effect on superoxide radicals, as well as the inhibition of hydrogen peroxide induced haemolysis. CPS1 showed a high antioxidant effect, especially scavenging effect of hydroxyl radicals, the reducing power and Fe(2+)-chelating activity. The results provide scientific support for the antioxidant activity and indicated a connection between antioxidant activity and reparation of renal failure.

PMID: 19885957 [PubMed - indexed for MEDLINE]

[J Altern Complement Med.](#) 2007 Jan-Feb;13(1):103-9.

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

[Wojcikowski K](#), [Stevenson L](#), [Leach D](#), [Wohlmuth H](#), [Gobe G](#).

Molecular and Cellular Pathology, School of Medicine, University of Queensland, Brisbane, Queensland, Australia. kwojciko@scu.edu.au

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]

[J Pharm Pharmacol](#). 2009 Mar;61(3):279-91.

Cordyceps fungi: natural products, pharmacological functions and developmental products.

[Zhou X](#), [Gong Z](#), [Su Y](#), [Lin J](#), [Tang K](#).

Plant Biotechnology Research Center, School of Agriculture and Biology, Shanghai Jiaotong University, Shanghai, PR China. xanweizhou@sjtu.edu.cn

Abstract

OBJECTIVES: Parasitic Cordyceps fungi, such as *Cordyceps sinensis*, is a parasitic complex of fungus and caterpillar, which has been used for medicinal purposes for centuries particularly in China, Japan and other Asian countries. This article gives a general idea of the latest developments in *C. sinensis* research, with regard to the active chemical components, the pharmacological effects and the research and development of products in recent years.

KEY FINDINGS: The common names for preparations include DongChongXiaCao in Chinese, winter worm summer grass in English. It has many bioactive components, such as 3'-deoxyadenosine, cordycepic acid and Cordyceps polysaccharides. It is commonly used to replenish the kidney and soothe the lung, and for the treatment of fatigue. It also can be used to treat conditions such as night sweating, hyposexuality, hyperglycaemia, hyperlipidaemia, asthenia after severe illness, respiratory disease, renal dysfunction, renal failure, arrhythmias and other heart disease and liver disease. Because of its rarity and outstanding curative effects, several mycelia strains have been isolated from natural Cordyceps and manufactured by fermentation technology, and are commonly sold as health food products. In addition, some substitutes such as *C. militaris* and adulterants also have been used; therefore, quality control of *C. sinensis* and its products is very important to ensure their safety and efficacy.

SUMMARY: Recent research advances in the study of Cordyceps, including Cordyceps mushrooms, chemical components, pharmacological functions and developmental products, has been reviewed and discussed. Developing trends in the field have also been appraised.

PMID: 19222900 [PubMed - indexed for MEDLINE]

[Zhongguo Zhong Xi Yi Jie He Za Zhi](#). 2009 Nov;29(11):975-8.

[Clinical application and exploration on mechanism of action of Cordyceps sinensis mycella prepration for renal transplantation recipients]

[Article in Chinese]

[Ding CG](#), [Tian PX](#), [Jin ZK](#).

The First Affiliated Hospital, Medical College of Xi'an Jiaotong University, Xi'an.

Abstract

OBJECTIVE: To retrospectively study and analyse the immune regulatory effect of Bailing Capsule (BLC, a dry powder preparation of Cordyceps sinensis mycelia) on patients after renal transplantation, its influences on various systems of organism, and to explore its possible acting mechanism.

METHODS: In accordance with the entry criteria, 67 recipients of renal homo-allograft were assigned to two groups. The 42 cases in the control group were treated with mycophenolate mofetil (MMF) plus cyclosporine A (CsA), or tacrolimus (FK506) plus prednisone (Pred); the 25 in the treated group treated with the chemotherapy the same as in the control group plus BLC. They were followed up for 48 weeks by checking up blood routine, urine routine, hepatic and renal function, total serum protein, serum albumin, uric acid, etc., and the dosage of immunoinhibitors used was recorded periodically.

RESULTS: Comparison showed no significant difference in graft survival rate, occurrence of reject reaction and renal function recovery between the two groups; but levels of urinary erythrocytes and leucocytes, blood alanine transaminase, aspartate amino transferase, uric acid, total bilirubin, direct bilirubin, as well as the incidence of infection were significantly lower, and serum total protein and albumin were significantly higher in the treated group (all $P < 0.01$); moreover, counts of erythrocyte and leukocyte from 12 to 48 weeks, T-lymphocyte from 4 to 48 weeks after transplantation were significantly higher in the treated group ($P < 0.05$ and $P < 0.01$), and the recovery appeared earlier, the dosage of CsA or FK506 used 12 weeks after operation was significantly lower in the treated group than in the control group ($P < 0.05$, $P < 0.01$).

CONCLUSIONS: BLC could effectively protect liver and kidney, stimulate hemopoietic function, improve hypoproteinemia, as well as reduce the incidence of infection and the dosage of CsA and FK506 used, etc. Therefore, it is a useful drug for immunoregulation after organ transplantation.

PMID: 20329604 [PubMed - in process]

[J Pharm Biomed Anal.](#) 2006 Aug 28;41(5):1571-84. Epub 2006 Feb 28.

Quality control of *Cordyceps sinensis*, a valued traditional Chinese medicine.

[Li SP](#), [Yang FQ](#), [Tsim KW](#).

Institute of Chinese Medical Sciences, University of Macau, Taipa, Macau SAR, China. SPLI@UMAC.MO

Abstract

Cordyceps sinensis, a well-known and valued traditional Chinese medicine, is also called DongChongXiaCao (winter worm summer grass) in Chinese. It is commonly used to replenish the kidney and soothe the lung for the treatment of fatigue, night sweating, hyposexualities, hyperglycemia, hyperlipidemia, asthenia after severe illness, respiratory disease, renal dysfunction and renal failure, arrhythmias and other heart disease, and liver disease. As the rarity and upstanding curative effects of natural *Cordyceps*, several mycelial strains have been isolated from natural *Cordyceps* and manufactured in large quantities by fermentation technology, and they are commonly sold as health food products in Asia. In addition, some substitutes such as *Cordyceps militaris* also have been used and adulterants also confused the market. Therefore, quality control of *C. sinensis* and its products is very important to ensure their safety and efficacy. Herein, markers and analytical methods for quality control of *Cordyceps* were reviewed and discussed.

PMID: 16504449 [PubMed - indexed for MEDLINE]

[Am J Chin Med.](#) 2005;33(3):491-500.

The nephroprotective effects of the herbal medicine preparation, WH30+, on the chemical-induced acute and chronic renal failure in rats.

[Ngai HH](#), [Sit WH](#), [Wan JM](#).

Division of Food and Nutritional Sciences, Department of Zoology The University of Hong Kong, Hong Kong SAR, P.R. China.

Abstract

In this study, we evaluated the renal protective effects of a Chinese herbal preparation WH30+ in male Wistar rats with glycerol-induced acute renal failure and adenine-induced chronic renal failure. WH30+ is a Chinese herb preparation composed of Rheum Palmatum, Salvia Miltiorrhiza, Cordyceps Sinensis, Leonurus Sibiricus, Epipedium Macranthum, Radix Astragali, and Radix Codonopsis Pilosulae, which has been used to treat kidney deficiency in human. An acute renal failure and chronic renal failure rat model were introduced by glycerol injection (i.m.) and fed with adenine-excessive diet, respectively. WH30+ was administered to rats at the dose of 50 mg/kg/day from 10 days before the diseases were induced until the rats were sacrificed. A reduction in body weight ($p < 0.01$) was observed in rats with chronic renal failure, but there was no difference between treatment groups. However, the body weight of rats with acute renal failure without treatment was significantly lower than those treated with WH30+ ($p < 0.05$). Overall, serum creatinine and urea nitrogen were elevated significantly ($p < 0.01$) in renal failure rats compared to control. Treatment with WH30+ improved both serum creatinine and urea nitrogen slightly in both models. The WH30+-treated rats with acute renal failure had significantly ($p < 0.05$) greater creatinine clearance than those without treatment. The results of the study show that WH30+ is more effective in the prevention of acute renal failure than chronic renal failure.

PMID: 16047565 [PubMed - indexed for MEDLINE]

[Nephrology \(Carlton\)](#). 2004 Dec;9(6):400-5.

Medicinal herbal extracts--renal friend or foe? Part two: herbal extracts with potential renal benefits.

[Wojcikowski K](#), [Johnson DW](#), [Gobé G](#).

School of Medicine, University of Queensland, Brisbane, Queensland, Australia. kwojciko@scu.edu.au

Abstract

In this second of two articles regarding the renal toxicities or benefits of medicinal herbs, herbs are reported as being 'potentially beneficial' to the kidneys if there is strong in vivo evidence of renal protection from toxic substances or drugs; potent, specific renal anti-oxidant effects; in vivo cancer antiproliferative effects specific to the kidneys; or in vivo evidence of being beneficial in renal disease or failure. Among the herbs, polyherbal formulae and fungi with potential renal benefits are Cordyceps sinensis, Sairei-to, Rheum spp., Salvia miltiorrhiza and its component, magnesium lithospermate B and others.

PMID: 15663644 [PubMed - indexed for MEDLINE]

L-arginina

[J Ren Nutr.](#) 2010 May;20(3):158-68. Epub 2010 Jan 25.

L-arginine and antioxidant diet supplementation partially restores nitric oxide-dependent regulation of phenylephrine renal vasoconstriction in diabetics rats.

[Coronel I](#), [Arellano-Mendoza MG](#), [del Valle-Mondragon L](#), [Vargas-Robles H](#), [Castorena-Torres F](#), [Romo E](#), [Rios A](#), [Escalante B](#).

Department of Molecular Biomedicine, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Mexico City, Mexico.

Abstract

OBJECTIVE: The increase of reactive oxygen species (ROS) in diabetes potentiates the vascular effects of phenylephrine through nitric oxide (NO) impairment, facilitating the development of diabetic nephropathy. We propose that the combination of an antioxidant and L-arginine as diet supplements could prevent the increased vascular response to phenylephrine in diabetic animals.

DESIGN: Changes in the adrenergic system play an important role in the development of vascular complications in the prediabetic condition. The vasoconstrictor effects of phenylephrine are regulated by NO, and the impairment of endothelium-dependent vasodilation in diabetes is associated with ROS.

SETTING: Diabetes was induced with a low dose (55 mg/kg body weight) of streptozotocin in 7-week-old rats. Diabetic rats were fed with a diet supplement containing a combination of vitamin E, vitamin C, eicosapentaenoic acid, docosahexaenoic acid, and L-arginine, and the effects on phenylephrine-induced renal vascular responses were evaluated.

RESULTS: Phenylephrine increased the renal perfusion pressure of isolated perfused kidneys from diabetic rats compared with nondiabetic rats. This effect was associated with reduced nitrite release as well as reduced plasma tetrahydrobiopterin and increased superoxide anions in the renal tissue. Diet supplementation with a combination of L-arginine and vitamins in diabetic rats partially prevented the generation of superoxide associated with recovery of the renal release of NO and decreased phenylephrine-induced vasoconstrictor effects, compared with untreated diabetic rats. However, the administration of L-arginine or vitamins alone did not affect phenylephrine-induced vasoconstriction. Vitamin treatment alone did decrease superoxide generation.

CONCLUSION: The protective mechanism of NO on the vasoconstrictor effects of phenylephrine in the kidney is lost during the development of diabetes, probably via the actions of ROS through a decrease in tetrahydrobiopterin, thus contributing to the pathogenesis of diabetic nephropathy. Restoration of this protective NO mechanism can be achieved by simultaneously stimulating NO synthesis and preventing the effects of ROS through the use of L-arginine and a combination of vitamins E and C as diet supplementation.

PMID: 20097580 [PubMed - indexed for MEDLINE]

[Chin J Physiol.](#) 2009 Oct 31;52(5):306-15.

Protective effects of L-arginine supplementation against exhaustive exercise-induced oxidative stress in young rat tissues.

[Huang CC](#), [Lin TJ](#), [Lu YF](#), [Chen CC](#), [Huang CY](#), [Lin WT](#).

Agricultural Biotechnology Research Center, Academia Sinica, Taipei 11529, Taiwan, ROC.

Abstract

Recently, we showed that L-arginine (L-Arg) supplementation could attenuate acute exercise-induced oxidative and inflammatory stress in aging rats. In this study, we investigate whether L-Arg supplementation protects cellular oxidative stress, inflammation, or the mitochondrial DNA 4834-bp large deletion (mtDNA4834 deletion) in 14-week-old young rats tissues during exhaustive exercise. Rats were randomly divided into four groups: sedentary control (SC); SC with L-Arg treatment (SC+Arg); exhaustive exercise (E); and exhaustive exercise with L-Arg treatment (E+Arg). Rats in the SC+Arg and E+Arg groups received supplemental 2% L-Arg diet. Rats in groups E and E+Arg performed an exhaustive running test on a treadmill. The results showed a significant increase in xanthine oxidase (XO) and myeloperoxidase (MPO) activities and lipid peroxide (malondialdehyde; MDA) levels of muscular, hepatic, and renal tissues in exercised rats as compared with sedentary rats. The increased XO, MPO, and MDA levels of these tissues significantly decreased in exercised rats supplemented with L-Arg. However, exhaustive exercise had no effect on mtDNA4834 deletions of muscular and hepatic tissues. The activities of creatine kinase (CK), aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine (CRE), lactate, uric acid, non-esterified fatty acid (NEFA), and D-3-hydroxybutyrate in the plasma significantly increased in the exercised rats compared with the sedentary rats, while the CK, lactate and uric acid levels in the plasma significantly decreased in L-Arg-supplemented exercised rats. These findings suggest that L-Arg supplementation reduces the oxidative damage to and inflammatory response in skeletal muscles, the liver, and kidneys caused by exhaustive exercise in young rats.

PMID: 20034235 [PubMed - indexed for MEDLINE]

[Amino Acids](#). 2009 May;37(1):153-68. Epub 2008 Nov 23.

Arginine metabolism and nutrition in growth, health and disease.

[Wu G](#), [Bazer FW](#), [Davis TA](#), [Kim SW](#), [Li P](#), [Marc Rhoads J](#), [Carey Satterfield M](#), [Smith SB](#), [Spencer TE](#), [Yin Y](#).

Department of Animal Science, Texas A&M University, College Station, TX 77843, USA. g-wu@tamu.edu

Abstract

L-Arginine (Arg) is synthesised from glutamine, glutamate, and proline via the intestinal-renal axis in humans and most other mammals (including pigs, sheep and rats). Arg degradation occurs via multiple pathways that are initiated by arginase, nitric-oxide synthase, Arg:glycine amidinotransferase, and Arg decarboxylase. These pathways produce nitric oxide, polyamines, proline, glutamate, creatine, and agmatine with each having enormous biological importance. Arg is also required for the detoxification of ammonia, which is an extremely toxic substance for the central nervous system. There is compelling evidence that Arg regulates interorgan metabolism of energy substrates and the function of multiple organs. The results of both experimental and clinical studies indicate that Arg is a nutritionally essential amino acid (AA) for spermatogenesis, embryonic survival, fetal and neonatal growth, as well as maintenance of vascular tone and hemodynamics. Moreover, a growing body of evidence clearly indicates that dietary supplementation or intravenous administration of Arg is beneficial in improving reproductive, cardiovascular, pulmonary, renal, gastrointestinal, liver and immune functions, as well as facilitating wound healing, enhancing insulin sensitivity, and maintaining tissue integrity. Additionally, Arg or L-citrulline may provide novel and effective therapies for obesity, diabetes, and the metabolic syndrome. The effect of Arg in treating many developmental and health problems is unique among AAs, and offers great promise for improved health and wellbeing of humans and animals.

PMID: 19030957 [PubMed - indexed for MEDLINE]

Urtica dioica

[Int Urol Nephrol](#). 2007;39(4):1137-46. Epub 2007 Feb 15.

Efficacy and safety of a combination of Sabal and Urtica extract in lower urinary tract symptoms--long-term follow-up of a placebo-controlled, double-blind, multicenter trial.

[Lopatkin N](#), [Sivkov A](#), [Schl fke S](#), [Funk P](#), [Medvedev A](#), [Engelmann U](#).

Institute of Urology, 3rd Parkovaya Street 51, 105425, Moscow, Russia, avsvkoff@yandex.ru.

Abstract

In an open-label extension of a randomized, double-blind clinical trial, the long-term efficacy and tolerability of a fixed combination of 160 mg Sabal fruit extract WS 1473 and 120 mg Urtica root extract WS 1031 per capsule (PRO 160/120) were investigated in elderly men with moderate or severe lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH). Two hundred and fifty-seven patients were randomly treated with 2 x 1 capsule/day PRO 160/120 or placebo for 24 weeks, followed by a 24-week control period and a 48-week follow-up period in which all patients received PRO 160/120. Efficacy measures included the assessment of LUTS [International Prostate Symptom Score ((I-PSS) self-rating questionnaire] and uroflow and sonographic parameters. Two hundred and nineteen subjects participated in the follow-up. Between baseline and end of observation (week 96) the I-PSS total score was reduced by 53% ($P < 0.001$), peak and average urinary flow increased by 19% ($P < 0.001$), and residual urine volume decreased by 44% ($P = 0.03$). The incidence of adverse events during follow-up was one in 1,181 treatment days; in only one event a causal relationship with intake of PRO 160/120 could not be excluded. Treatment with PRO 160/120 thus provides a clinically relevant benefit over a period of 96 weeks.

PMID: 18038253 [PubMed - indexed for MEDLINE]

[World J Urol.](#) 2002 Nov;20(5):285-93. Epub 2002 Oct 17.

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]

[Planta Med.](#) 2001 Aug;67(6):489-500.

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.

[Koch E.](#)

Department of Pharmacology, Dr. Willmar Schwabe Arzneimittel GmbH, Karlsruhe, Germany.

egon.koch@schwabe.de

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 particular, 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]

[J Ethnopharmacol](#). 2000 Nov;73(1-2):95-100.

Acute diuretic, natriuretic and hypotensive effects of a continuous perfusion of aqueous extract of *Urtica dioica* in the rat.

[Tahri A](#), [Yamani S](#), [Legssyer A](#), [Aziz M](#), [Mekhfi H](#), [Bnouham M](#), [Ziyyat A](#).

Laboratoire de Physiologie et Pharmacologie Cellulaire, Faculté des Sciences, Université Mohammed Premier, B.P. 524, 60000, Oujda, Morocco. atahri@sciences.univ-oujda.ac.ma

Abstract

This study was performed on anaesthetized male Wistar rats that received a continuous intravenous perfusion during 1.25 h of an aqueous extract of aerial parts of *Urtica dioica* L. (Urticaceae) at a low dose of 4 mg/kg/h or at a high dose of 24 mg/kg/h, or furosemide (control diuretic) at a dose of 2 mg/kg/h. As compared with a control period in each rat, the arterial blood pressure was reduced proportionally to the dose of the perfusion of the plant extract (15 and 38%, $P < 0.001$, respectively). These effects were accompanied by a correlative increase of diuresis (11 and 84%, $P < 0.001$, respectively) and natriuresis (28 and 143%, $P < 0.001$, respectively). In the rats perfused by furosemide, the arterial blood pressure was reduced by 28% ($P < 0.001$). The diuresis and natriuresis were also increased proportionally in this case (85 and 155%, $P < 0.001$, respectively). Nevertheless, the hypotensive action of *U. dioica* was reversible during the recovery periods in about 1 h with the lower dose of the plant extract and furosemide, while the effect of the higher dose was persistent, indicating a possible toxic effect. In conclusion, the results demonstrate an acute hypotensive action of *U. dioica* that indicates a direct effect on the cardiovascular system. Moreover, diuretic and natriuretic effects were also observed, suggesting an action on the renal function. Finally, the plant extract seems to have a toxic effect at the higher dose.

PMID: 11025144 [PubMed - indexed for MEDLINE]

Inositol

[Physiol Rev.](#) 1991 Oct;71(4):1081-115.

Renal medullary organic osmolytes.

[Garcia-Perez A](#), [Burg MB](#).

Laboratory of Kidney and Electrolyte Metabolism, National Heart, Lung, and Blood Institute, Bethesda, Maryland.

Abstract

Sorbitol, inositol, GPC, and betaine are the predominant organic osmolytes in renal medullary cells. They protect the cells from harmful effects of the high interstitial NaCl and urea concentrations that occur normally in the renal medulla with operation of the urinary concentrating mechanism. Their levels correlate with extracellular NaCl concentration and, in the case of GPC, also with urea. Sorbitol is synthesized from glucose in a reaction catalyzed by aldose reductase. Inositol and betaine are transported into the cell. Glycerophosphorylcholine synthesis is dependent on choline. The transcription of aldose reductase and the transport of betaine and inositol are regulated, dependent on the degree of hypertonicity. Normal organic osmolyte regulation contributes to the survival and growth of medullary cells in their hyperosmolal environment, and defective regulation can damage them.

PMID: 1924548 [PubMed - indexed for MEDLINE]

[Am J Physiol.](#) 1990 Nov;259(5 Pt 2):F847-58.

Factors affecting the ratio of different organic osmolytes in renal medullary cells.

[Moriyama T](#), [Garcia-Perez A](#), [Burg MB](#).

Laboratory of Kidney and Electrolyte Metabolism, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland 20892.

Abstract

Renal medullary cells contain high concentrations of sorbitol, inositol, glycerophosphorylcholine (GPC), and betaine, which balance the variably high osmolality of extracellular NaCl. We found that PAP-HT25 (rabbit renal medullary) cells in tissue culture increase their content of all four when medium osmolality is increased by adding NaCl and urea. However, this requires that betaine be added to medium in addition to customary constituents. Some factors affecting the mix of organic osmolytes in these cells during hypertonicity are as follows. 1) Urea in medium increases cell GPC and tends to decrease others, particularly betaine. 2) With small increases in medium NaCl, intracellular inositol is highest, whereas sorbitol predominates with large NaCl increases. 3) When osmolality is suddenly decreased, these four organic osmolytes exit rapidly from cells, but in differing relative amounts (betaine much greater than sorbitol greater than inositol much greater than GPC). 4) Altering cell betaine levels (by varying betaine in medium) causes reciprocal changes in cell sorbitol (by affecting aldose reductase activity) and vice versa, whereas inositol and GPC are less affected. 5) Raising medium glucose concentration (from which sorbitol is synthesized) increases cell sorbitol and decreases cell inositol and betaine. 6) Decreasing the amount of GPC in cells (by removing choline from medium) causes small changes in betaine and sorbitol, but not in inositol. Changing the amount of inositol does not affect the others. Similar interrelations may operate in vivo to vary the mix of organic osmolytes in renal medulla.

PMID: 2240234 [PubMed - indexed for MEDLINE]

Vitaminas Grupo B

[Diabetologia](#). 2010 Jul;53(7):1506-16. Epub 2010 Apr 6.

Increased protein damage in renal glomeruli, retina, nerve, plasma and urine and its prevention by thiamine and benfotiamine therapy in a rat model of diabetes.

[Karachalias N](#), [Babaei-Jadidi R](#), [Rabbani N](#), [Thornalley PJ](#).

Department of Biological Sciences, University of Essex, Central Campus, Wivenhoe Park, Colchester, Essex, UK.

Abstract

AIMS/HYPOTHESIS: The aim of this study was to quantify protein damage by glycation, oxidation and nitration in a rat model of diabetes at the sites of development of microvascular complications, including the effects of thiamine and benfotiamine therapy.

METHODS: Diabetes was induced in male Sprague-Dawley rats by 55 mg/kg streptozotocin and moderated by insulin (2 U twice daily). Diabetic and control rats were given thiamine or benfotiamine (7 or 70 mg kg⁻¹ day⁻¹) over 24 weeks. Plasma, urine and tissues were collected and analysed for protein damage by stable isotopic dilution analysis MS.

RESULTS: There were two- to fourfold increases in fructosyl-lysine and AGE content of glomerular, retinal, sciatic nerve and plasma protein in diabetes. Increases in AGEs were reversed by thiamine and benfotiamine therapy but increases in fructosyl-lysine were not. Methionine sulfoxide content of plasma protein and 3-nitrotyrosine content of sciatic nerve protein were increased in diabetes. Plasma glycation free adducts were increased up to twofold in diabetes; the increases were reversed by thiamine. Urinary excretion of glycation, oxidation and nitration free adducts was increased by seven- to 27-fold in diabetes. These increases were reversed by thiamine and benfotiamine therapy.

CONCLUSIONS/INTERPRETATION: AGEs, particularly arginine-derived hydroimidazolones, accumulate at sites of microvascular complication development and have markedly increased urinary excretion rates in experimental diabetes. Thiamine and benfotiamine supplementation prevented tissue accumulation and increased urinary excretion of protein glycation, oxidation and nitration adducts. Similar effects may contribute to the reversal of early-stage clinical diabetic nephropathy by thiamine.

PMID: 20369223 [PubMed - indexed for MEDLINE]

Vitamin B6 and oxalic acid in clinical nephrology.

[Mydlík M,](#) [Derzsiova K.](#)

IVth Internal Clinic, Hospital of L. Pasteur, Medical School of P. J. Safárik University, Kosice, Slovak Republic. k.derzsiova@fnlp.sk

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.

[Urol Res.](#) 2007 Aug;35(4):173-8. Epub 2007 Jun 13.

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

[Teerajetgul Y](#), [Hossain RZ](#), [Yamakawa K](#), [Morozumi M](#), [Sugaya K](#), [Ogawa Y](#).

Division of Urology, Department of Organ-oriented Medicine, Faculty of Medicine, University of the Ryukyus, 207 Uehara, Nishihara, Okinawa 903-0215, Japan.

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.

PMID: 17565492 [PubMed - indexed for MEDLINE]

[Nutr Hosp.](#) 2007 Jan-Feb;22(1):7-24.

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

[Spinneker A](#), [Sola R](#), [Lemmen V](#), [Castillo MJ](#), [Pietrzik K](#), [González-Gross M](#).

Grupo Effects 262, Facultad de Medicina, Universidad de Granada, Spain.

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.ncbi.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]

[J Nutr Health Aging](#). 2002;6(1):39-42.

Folate, vitamin B12 and vitamin B6 and one carbon metabolism.

[Selhub J.](#)

JM USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA, USA.

jsselhub@hnrc.tufts.edu

Abstract

The vitamins folic acid, B12 and B6 and B2 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 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.

PMID: 11813080 [PubMed - indexed for MEDLINE]

[J Urol.](#) 1999 Jun;161(6):1748-60.

Chemoprevention of urological cancer.

[Kamat AM](#), [Lamm DL](#).

Department of Urology, West Virginia University School of Medicine, Morgantown, USA.

Comment in: [J Urol.](#) 2000 Apr;163(4):1260-1.

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.

PMID: 10332429 [PubMed - indexed for MEDLINE]

[Gesundheitswesen](#). 1997 Apr;59(4):248-51.

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

[Article in German]

[Hort A](#), [Brand H](#).

Behörde für Arbeit, Gesundheit und Soziales, Hamburg.

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 important 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.

PMID: 9296731 [PubMed - indexed for MEDLINE]

[Metabolism](#). 1979 May;28(5):542-8.

Primary oxalosis: clinical and biochemical response to high-dose pyridoxine therapy.

[Will EJ](#), [Bijvoet OL](#).

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 $\mu\text{mole/liter}$ after 15 mo of treatment. The decrease in glycollic 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]