

**Vinpocetine treatment in acute ischaemic stroke: a pilot single-blind randomized clinical trial.**

Feigin VL, Doronin BM, Popova TF, et al. *Eur J Neurol* 2001;8:81-85.

The aim of the study was to assess the safety and feasibility of a clinical trial on the effect of vinpocetine, a synthetic ethyl ester of apovincamine, in acute ischaemic stroke. Thirty consecutive patients with computed tomography verified diagnosis of acute ischaemic stroke, who could receive drug treatment within 72 h of stroke onset, were enrolled. The patients were randomly allocated to receive either low-molecular weight dextran alone or in combination with vinpocetine. Poor outcome was defined as being dead or having a Barthel index of < 70 or a Rankin score of 3-5. Intention-to-treat analysis was applied. One-tenth of all hospitalized patients with acute ischaemic stroke were eligible for the trial. Thirty eligible patients were treated with either low-molecular weight dextran alone (mean age 57.9 +/- 11.6 years, n = 15) or in combination with vinpocetine (mean age 60.8 +/- 6.6 years, n = 15). The two treatment groups were comparable with respect to major prognostic variables. A relative risk (RR) reduction of poor outcome at 3 months follow-up was 30% (RR = 0.7; 95% confidence interval [CI] 0.1-3.4), as defined by the modified Barthel Index, and 60% as defined by the modified Ranking score (RR = 0.4, 95% CI: 0.1-1.7). The National Institute of Health (NIH-NINDS) Stroke Scale score was marginally significantly better in the vinpocetine treated group at 3 months of follow-up (P = 0.05, ANOVA). No significant adverse effects were seen. This pilot study shows that a full-scale randomized double-blind, placebo-controlled trial of vinpocetine treatment in acute ischaemic stroke is feasible and warranted.

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### **Short- and long-term black tea consumption reverses endothelial dysfunction in patients with coronary artery disease.**

Duffy SJ, Keaney JF Jr, Holbrook M, et al.

*Circulation* 2001;104:151-156.

**BACKGROUND:** Epidemiological studies suggest that tea consumption decreases cardiovascular risk, but the mechanisms of benefit remain undefined. Endothelial dysfunction has been associated with coronary artery disease and increased oxidative stress. Some antioxidants have been shown to reverse endothelial dysfunction, and tea contains antioxidant flavonoids. **METHODS AND RESULTS:** To test the hypothesis that tea consumption will reverse endothelial dysfunction, we randomized 66 patients with proven coronary artery disease to consume black tea and water in a crossover design. Short-term effects were examined 2 hours after consumption of 450 mL tea or water. Long-term effects were examined after consumption of 900 mL tea or water daily for 4 weeks. Vasomotor function of the brachial artery was examined at baseline and after each intervention with vascular ultrasound. Fifty patients completed the protocol and had technically suitable ultrasound measurements. Both short- and long-term tea consumption improved endothelium-dependent flow-mediated dilation of the brachial artery, whereas consumption of water had no effect ( $P < 0.001$  by repeated-measures ANOVA). Tea consumption had no effect on endothelium-independent nitroglycerin-induced dilation. An equivalent oral dose of caffeine (200 mg) had no short-term effect on flow-mediated dilation. Plasma flavonoids increased after short- and long-term tea consumption. **CONCLUSIONS:** Short- and long-term black tea consumption reverses endothelial vasomotor dysfunction in patients with coronary artery disease. This finding may partly explain the association between tea intake and decreased cardiovascular disease events.

### **The chronic effects of an extract of *Bacopa monniera* (Brahmi) on cognitive function in healthy human subjects.**

Stough C, Lloyd J, Clarke J, et al. *Psychopharmacology* 2001;156:481-484.

**RATIONALE:** Extracts of *Bacopa monniera* have been reported to exert cognitive enhancing effects in animals. However, the effects on human cognition are inconclusive. **OBJECTIVE:** The current study examined the chronic effects of an extract of *B. monniera* (Keenmind) on cognitive function in healthy human subjects. **METHODS:** The study was a double-blind placebo-controlled independent-group design in which subjects were randomly allocated to one of two treatment conditions, *B. monniera* (300 mg) or placebo. Neuropsychological testing was conducted pre-(baseline) and at 5 and 12 weeks post drug administration. **RESULTS:** *B. monniera* significantly improved speed of visual information processing measured by the IT task, learning rate and memory consolidation measured by the AVLT ( $P < 0.05$ ), and state anxiety ( $P < 0.001$ ) compared to placebo, with maximal effects evident after 12 weeks. **CONCLUSIONS:** These findings suggest that *B. monniera* may improve higher order cognitive processes that are critically dependent on the input of information from our environment such as learning and memory.

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### **Experience with St John's wort (*Hypericum perforatum*) in children under 12 years with symptoms of depression and psychovegetative disturbances.**

Hubner WD, Kirste T. *Phytother Res* 2001;15:367-370.

The value of an extract of *Hypericum perforatum* (St John's wort) for children with mild to moderate depressive symptoms was investigated for the first time in a multi-centre post-marketing surveillance study. One hundred and one children under 12 years were treated for a minimum of 4 weeks with an extension to 6 weeks with parental consent and medical practitioner recommendation. The dosage used ranged from 300 to 1800 mg per day. Compliance, tolerability and efficacy were assessed every 2 weeks by physicians and parents. Based on the data available for analysis, the number of physicians rating effectiveness as 'good' or 'excellent' was 72% after 2 weeks, 97% after 4 weeks and 100% after 6 weeks. The ratings by parents were very similar. There was, however, an increasing amount of missing data at each assessment point with the final evaluation including only 76% of the initial sample. Tolerability was good and no adverse events were reported. The results of this study suggest that *Hypericum* is a potentially safe and effective treatment for children with symptoms of depression.

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### **Dietary probiotic supplementation enhances natural killer cell activity in the elderly: an investigation of age-related immunological changes.**

Gill HS, Rutherford KJ, Cross ML. *J Clin Immunol* 2001;21:264-271.

Many elderly subjects are at increased risk of infectious and noninfectious diseases due to an age-related decline in lymphoid cell activity (immunosenescence). Noninvasive means of enhancing cellular immunity are therefore desirable in the elderly. Previous reports have suggested that dietary supplementation could represent an effective means of enhancing the activity of circulating natural killer (NK) cells in the elderly. In the present study, we have conducted a pre-post intervention trial to determine the impact of dietary supplementation with probiotic lactic acid bacteria (LAB) on peripheral blood NK cell activity in healthy elderly subjects. Twenty-seven volunteers consumed low-fat/low-lactose milk supplemented with known immunostimulatory LAB strains (*Lactobacillus rhamnosus* HN001 or *Bifidobacterium lactis* HN019) for a period of 3 weeks. A dietary run-in of milk alone was shown to have no significant effect on NK cells. In contrast, the proportion of CD56-positive lymphocytes in peripheral circulation was higher following consumption of either LAB strain, and ex vivo PBMC tumoricidal activity against K562 cells was also increased. Supplementation with HN001 or HN019 increased tumoricidal activity by an average of 101 and 62%, respectively; these increases were significantly correlated with age, with subjects older than 70 years experiencing significantly greater improvements than those under 70 years. These results demonstrate that dietary consumption of probiotic LAB in a milk-based diet may offer benefit to elderly consumers to combat some of the deleterious effects of immunosenescence on cellular immunity.

**Efficacy and tolerability of Hypericum extract WS 5572 versus placebo in mildly to moderately depressed patients. A randomized double-blind multicenter clinical trial.**

Kalb R, Trautmann-Sponsel RD, Kieser M.

*Pharmacopsychiatry*  
2001;34:96-103.

We have investigated the antidepressant efficacy and safety of Hypericum perforatum (St. John's wort) extract WS5572 in a double-blind, placebo-controlled multicenter clinical trial. 72 patients (WS 5572: 37, placebo: 35) with a diagnosis of mild to moderate major depressive disorder (according to DSM-IV criteria) were randomized in 42 days of treatment with either 300 mg WS5572 t.i.d. or placebo. The primary efficacy variable was the change of the 17-item Hamilton Depression Scale (HAMD) total score between baseline and double-blind treatment. The study was conducted with an adaptive interim analysis, which led to early stopping because convincing treatment efficacy could already be demonstrated. Group differences in favor of WS 5572 were descriptively apparent as early as day 7 of randomized treatment and were statistically significant at days 28 ( $p = 0.011$ ) and day 42 ( $p < 0.001$ ). Between baseline and treatment end, the HAMD total score decreased from  $19.7 \pm 3.4$  to  $8.9 \pm 4.3$  points in the Hypericum group and from  $20.1 \pm 2.6$  to  $14.4 \pm 6.8$  points in the placebo group (mean  $\pm$  SD). Responder rates were consistently higher in the Hypericum group. Comparable group differences in favor of WS 5572 were also found for von Zerssen's Depression Scale (D-S; self-rating), Clinical Global Impressions (CGI) and a global patient's self-assessment (GPA). Tolerability was very good in both groups, with no adverse drug reactions and no clinically relevant changes in safety parameters. The results indicate that Hypericum extract WS 5572 is an effective and well-tolerated drug for the treatment of mild to moderate major depressive disorder.

### **Dietary soy has both beneficial and potentially adverse cardiovascular effects: a placebo-controlled study in men and postmenopausal women.**

Teede HJ, Dalais FS, Kotsopoulos D, et al. *J Clin Endocrinol Metab* 2001;86:3053-3060.

To address the cardiovascular effects of dietary soy containing phytoestrogens, we measured blood pressure (BP), lipids, vascular function (systemic arterial compliance and pulse wave velocity), and endothelial function (flow-mediated vasodilation) in a randomized, double-blind trial. Two hundred thirteen healthy subjects (108 men and 105 postmenopausal women), 50-75 yr old, received either soy protein isolate (40 g soy protein, 118 mg isoflavones) or casein placebo for 3 months. There were 34 withdrawals (16%), with 179 subjects (96 men and 83 women) completing the protocol. After intervention in the soy group, compared with casein placebo, urinary phytoestrogens increased, accompanied by a significant fall in BP reflected by the BP model ( $P < 0.01$ ) encompassing mean change ( $\pm$ SEM) in systolic ( $-7.5 \pm 1.2$  vs.  $-3.6 \pm 1.1$  mm Hg,  $P < 0.05$ ), diastolic ( $-4.3 \pm 0.8$  vs.  $-1.9 \pm 0.7$  mm Hg,  $P < 0.05$ ), and mean BP ( $-5.5 \pm 1$  vs.  $-0.9 \pm 1$  mm Hg,  $P < 0.008$ ). In the lipid model, soy induced greater changes, compared with placebo ( $P < 0.001$ ). On individual analysis, significant contributors included a reduction in the low- to high-density lipoprotein ratio ( $-0.33 \pm 0.1$  vs.  $0.04 \pm 0.1$  mmol/L,  $P < 0.05$ ) and triglycerides ( $-0.2 \pm 0.05$  vs.  $-0.01 \pm 0.05$  mol/L,  $P < 0.05$ ) and an increase in Lp(a) lipoprotein ( $\pm$  95% confidence interval) [42 (range, 17-67) vs. 4 (range, -22-31) mg/L,  $P < 0.05$ ], whereas total, low-density lipoprotein, and high-density lipoprotein cholesterol improved in both groups; but no treatment effect was demonstrated. The arterial functional model demonstrated no difference between groups; although again, overall function improved in both groups. On individual analysis, peripheral PWV (reflecting peripheral vascular resistance) improved with soy ( $P < 0.01$ ), whereas flow-mediated vasodilation (reflecting endothelial function) declined (in males only), compared with casein placebo ( $P < 0.02$ ). No effect of treatment on the hypothalamic-pituitary-gonadal axis was noted in males or females. In normotensive men and postmenopausal women, soy improved BP and lipids but, overall, did not improve vascular function. Potential adverse effects were noted, with a decline in endothelial function (in males only) and an increase in Lp(a). Further research in hypertensive and hyperlipidemic populations is needed.

### **Efficacy of ipriflavone in preventing adverse effects of leuprolide.**

Somekawa Y, Chiguchi M, Ishibashi T, et al. *J Clin Endocrinol Metab* 2001;86:3202-3206.

The purpose of this study was to evaluate the efficacy of ipriflavone in preventing bone loss, decreasing in serum cholesterol and decreasing the rate of appearance of vasomotor symptoms, as well as the effects of ipriflavone on reduction of myoma volume by estrogen deficiency during treatment with the GnRH analog leuprolide. One hundred two women (mean age, 44.3 +/- 0.53 yr) receiving leuprolide therapy for uterine leiomyoma were randomly allocated to two groups (group A, leuprolide only; group B, leuprolide with ipriflavone). Bone mineral density of the lumbar spine was measured by dual-energy x-ray absorptiometry before and after treatment for 6 months. Levels of serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol (LDL-C) were measured before treatment and after 3 and 6 months of treatment. Subjects were asked to report the appearance of vasomotor symptoms throughout treatment. Myoma node volumes were measured before treatment and after treatment for 6 months. Bone mineral density was reduced in both groups, with reduction rates of -5.26% in group A and -3.70% in group B ( $P < 0.01$  vs. group A). Changes in bone markers were not significant in either group. TC was significantly increased in both groups, and TG levels were increased significantly after 3 and 6 months of treatment in group A but not in group B. There was no significant difference between these two groups in amount of increase of either TC or TG. LDL-C levels were increased significantly after 3 and 6 months of treatment in both groups, and the differences between the groups (11.7% in group A vs. 7.5% in group B at 3 month and 22.6% in group A vs. 8.4% in group B at 6 month) were significant. Severe vasomotor symptoms were reduced in group B. The rates of reduction of myoma volume were 49.8% in group A and 52.9% in group B; this difference between groups was not significant. Ipriflavone efficaciously alleviated the adverse effects of estrogen deficiency such as bone loss and increase in LDL-C level, and the ability of leuprolide therapy to reduce myoma volume was not decreased by ipriflavone administration.

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### **Heart rate variability and n-3 polyunsaturated fatty acids in patients with diabetes mellitus.**

Christensen JH, Skou HA, Madsen T, et al. *J Intern Med* 2001;249:545-552.

**OBJECTIVES:** Dietary n-3 polyunsaturated fatty acids (PUFA) derived from fish may reduce the incidence of sudden cardiac death (SCD). The aim of the present study was to examine associations between n-3 PUFA and 24-h heart rate variability in patients with type 1 and type 2 diabetes mellitus (DM). **DESIGN:** Observational study. **SETTING:** The out-patient's diabetic clinic at Hjørring Hospital, Hjørring, Denmark. **SUBJECTS:** Forty-three patients with type 1 DM and 38 patients with type 2 DM. **MAIN OUTCOME MEASURES:** The patients fulfilled a food-questionnaire regarding fish consumption, whilst the content of n-3 PUFA in platelets was measured and 24-h heart rate variability (HRV) was obtained. **RESULTS:** The patients fish consumption was strongly related to their content of n-3 PUFA in platelets. Furthermore, in patients with type 1 DM a close positive association was found between the content of n-3 PUFA in platelets and 24-h HRV. This association was not significant in patients with type 2 DM. **CONCLUSIONS:** The positive association between n-3 PUFA in platelets and HRV may indicate a beneficial effect of n-3 PUFA on HRV in patients with type 1 DM. Further studies are warranted to clarify whether supplementation with n-3 PUFA reduce the risk of SCD amongst patients with DM.

### **The effects of pantethine on fatty liver and fat distribution.**

Osono Y, Hirose N, Nakajima K, Hata Y. *J Atheroscler Thromb* 2000;7:55-58.

Although the prognosis of fatty liver depends on its causes, we feel from our clinical experience that fatty liver with hypertriglyceridemia has a good prognosis and responds well to treatment. In this study, 600 mg/day of pantethine was administered to 16 outpatients with fatty liver and hypertriglyceridemia for six months or longer to examine whether the drug improved fatty liver using abdominal plain computed tomography (CT). Nine of the 16-pantethine patients were no longer diagnosed as having fatty liver after the study period. An chi2 test indicated the significant disappearance of fatty liver. At the same time, the visceral fat calculated from the CT image passing the umbilical region was also significantly reduced. On the contrary, the subcutaneous fat area tended to increase, so the ratio of the visceral-to-subcutaneous fat area was reduced significantly. This indicates triglycerides may be pooled in the body as hepato-visceral fat and subcutaneous fat, and that pantethine may transfer fat from the liver and viscera to the subcutaneous tissue. This suggests that visceral fat deposition and fatty liver occurring with hypertriglyceridemia may have a common basis, probably excessive matrixes, and that pantethine may simultaneously improve the two conditions.

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### **Improvement of cognitive functions after cobalamin/folate supplementation in elderly patients with dementia and elevated plasma homocysteine.**

Nilsson K, Gustafson L, Hultberg B. *Int J Geriatr Psychiatry* 2001;16:609-614.

**OBJECTIVES:** To investigate the effect of cobalamin/folate supplementation on cognitive function in elderly patients with dementia. **METHOD:** The cobalamin/folate status of the patients was evaluated by measuring plasma homocysteine, serum methylmalonic acid, serum cobalamin and blood folate. Thirty-three patients were studied and repeatedly assessed with the Mini-Mental State Examination (MMSE) and 'A short cognitive performance test for assessing memory and attention' (SKT) during vitamin substitution. **RESULTS:** Patients with mild-moderate dementia and elevated plasma homocysteine levels improved clinically with increased test scores after vitamin substitution, while severely demented patients and patients with normal plasma homocysteine levels did not improve clinically. **CONCLUSIONS:** Plasma homocysteine may be the best marker for detecting treatable cobalamin/folate deficiency in patients with dementia.

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### **A pilot study on the relation between cisplatin neuropathy and vitamin E.**

Bove L, Picardo M, Maresca V, et al. *J Exp Clin Cancer Res* 2001;20:277-280.

Peripheral sensory neuropathy is the main non-hematological side-effect related to cisplatin chemotherapy. The strong similarity between clinical and neuropathological aspects in peripheral neuropathy induced by cisplatin and neurologic syndromes due to vitamin E deficiency, prompted us to investigate the relationship between cisplatin neuropathy and plasmatic level of vitamin E (alpha-tocopherol). We measured vitamin E in the plasma of 5 patients (Group 1) which developed severe neurotoxicity after cisplatin treatment and in another group of 5 patients (Group 2) we analyzed the plasmatic level of vitamin E before and after 2 or 4 cycles of cisplatin treatment. The results showed that the patients of group 1 presented low plasmatic levels of vitamin E and that the patients of group 2 presented significantly lower levels of vitamin E after 2 or 4 cycles of cisplatin than before treatment. Our preliminary data suggest that an inadequate amount of the antioxidant vitamin E due to cisplatin treatment could be responsible for the peripheral nerve damage induced by free-radicals. Given the lack of toxicity of vitamin E, we need to systematically assess the possible neuroprotective role of vitamin E supplementation in patients treated with cisplatin chemotherapy.

### **Evaluation of combining kava extract with hormone replacement therapy in the treatment of postmenopausal anxiety.**

De Leo V, la Marca A, Morgante G, et al. *Maturitas* 2001;39:185-188.

Objective: to evaluate the efficacy of combining kava extract with hormone replacement therapy in the treatment of menopausal anxiety. Materials and methods: HAMA score was evaluated before and after therapy in four groups of women in menopause (duration of menopause ranged from 1 to 12 years). The groups were treated with hormone replacement therapy (with and without progestogens) and kava extract or placebo for 6 months. Results: A significant reduction in HAMA score was observed in all four groups of women. The reduction was more significant in groups taking kava extract than in groups on hormones only. Discussion: The combined use of hormone replacement therapy and kava extract seems to be effective against menopausal anxiety. Kava extract accelerates resolution of psychological symptoms while hormone therapy safeguards against osteoporosis and cardiovascular disease.

### **Long-term clinical outcome in patients with glutathione synthetase deficiency.**

Ristoff E, Mayatepek E, Larsson A. *J Pediatr* 2001;139:79-84.

**OBJECTIVE:** The objective was to determine the long-term clinical outcome and the effects of treatment of patients with glutathione synthetase (GS) deficiency (n = 28). **METHODS:** The diagnosis was based on demonstration of a marked decrease in GS activity in erythrocytes or cultured fibroblasts in all patients and was supported by finding a decrease in erythrocyte or fibroblast glutathione, presence of 5-oxoprolinuria, or both. The treatment varied but usually included correction of acidosis and supplementation with vitamins C and/or E. **RESULTS:** Sixteen patients were severely affected with neurologic symptoms such as seizures and psychomotor retardation; 7 had died at the time of the study. None of the severely affected patients had been treated with both vitamins C and E from the neonatal period. No significant difference was found in GS activity between patients with or without neurologic symptoms or in erythrocyte or fibroblast glutathione levels. Five patients had recurrent bacterial infections. **CONCLUSION:** On the basis of clinical symptoms, patients with GS deficiency can be classified into 3 phenotypes: mild, moderate, and severe. Our results indicate that early supplementation with vitamins C and E may improve the long-term clinical outcome.

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### **Beneficial effects of alpha-lipoic acid and ascorbic acid on endothelium-dependent, nitric oxide-mediated vasodilation in diabetic patients: relation to parameters of oxidative stress.**

Heitzer T, Finckh B, Albers S, et al. *Free Radic Biol Med* 2001;31:53-61.

The impairment of nitric oxide (NO)-mediated vasodilation in diabetes has been attributed to increased vascular oxidative stress. Lipoic acid has been shown to have substantial antioxidative properties. The aim of this study was to assess the effect of lipoic acid on NO-mediated vasodilation in diabetic patients in comparison with the well-recognized effect of ascorbic acid. Using venous occlusion plethysmography, we examined the effects of lipoic acid (0.2 mM) and ascorbic acid (1 and 10 mM) on forearm blood flow responses to acetylcholine, sodium nitroprusside and concomitant infusion of the NO-inhibitor, N(G)-monomethyl-L-arginine, in 39 diabetic patients and 11 control subjects. Plasma levels of antioxidants and parameters of lipid peroxidation were measured and correlated to endothelial function tests. Lipoic acid improved NO-mediated vasodilation in diabetic patients, but not in controls. NO-mediated vasodilation was improved by ascorbic acid at 10 mM, but not 1 mM. Improvements of endothelial function by ascorbic acid and lipoic acid were closely related. The beneficial effects of lipoic acid were positively related to plasma levels of malondialdehyde and inversely related to levels of ubiquinol-10. These findings support the concept that oxidative stress contributes to endothelial dysfunction and suggest a therapeutic potential of lipoic acid particularly in patients with imbalance between increased oxidative stress and depleted antioxidant defense.

### **Dietary folate intake, alcohol, and risk of breast cancer in a prospective study of postmenopausal women.**

Sellers TA, Kushi LH, Cerhan JR, et al.

*Epidemiology* 2001;12:420-428.

Low B-vitamin intake may increase risk of breast cancer through decreased DNA repair capacity. Alcohol intake increases risk for breast cancer, with evidence from prospective studies of an interaction between alcohol and folate. We explored dietary intake of folate and other B vitamins with risk of breast cancer in a cohort study of 34,387 postmenopausal women. To measure diet, we mailed a food frequency questionnaire; we estimated nutrient intakes and categorized them into four levels: <10th, 11th-30th, 31st-50th, and >50th percentiles. Through 12 years of follow-up, we identified 1,586 cases of breast cancer in the cohort at risk. We estimated relative risks (RRs) and 95% confidence intervals (CIs) through Cox regression models adjusted for age, energy, and other risk factors. Women in the lowest 10th percentile of folate intake from diet alone were at modestly increased risk of breast cancer relative to those above the 50th percentile: RR = 1.21 (95% CI = 0.91-1.61). We examined the joint association of folate intake and alcohol use on risk of breast cancer, with the reference group defined as women with high folate (>50th percentile) and no alcohol use. The RRs of breast cancer associated with low dietary folate intake were 1.08 (95% CI = 0.78-1.49) among nondrinkers, 1.33 (95% CI = 0.86-2.05) among drinkers of < or = 4 gm per day, and 1.59 (95% CI = 1.05-2.41) among drinkers of > 4 gm per day. These results suggest that the risks of postmenopausal breast cancer may be increased among women with low intakes of folate if they consume alcohol-containing beverages.

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

Biagiotti G, Cavallini G.  
*BJU Int* 2001;88:63-67.

**OBJECTIVE:** To detect whether oral acetyl-L-carnitine might be useful in the acute and early chronic phases of Peyronie's disease, compared with tamoxifen, a drug currently in use. **PATIENTS AND METHODS:** The study included 48 patients with Peyronie's disease (15 acute and 33 initial chronic), randomized equally into two groups. The first group used tamoxifen 20 mg twice daily for 3 months and the second acetyl-L-carnitine 1 g twice daily for 3 months. The disease and stages were diagnosed and identified using a history, objective examination, pharmacologically induced erection, autophotography during erection, and basic and dynamic colour Doppler ultrasonography. Penile curvature, plaque size, pain and disease progression were assessed. The differences between the groups or between the variables before and after therapy were compared using analysis of variance or the chi-squared test. **RESULTS:** Acetyl-L-carnitine was significantly more effective than tamoxifen in reducing pain and in inhibiting disease progression. Acetyl-L-carnitine reduced penile curvature significantly, while tamoxifen did not; both drugs significantly reduced plaque size. Tamoxifen induced significantly more side-effects than acetyl-L-carnitine. **CONCLUSIONS:** These results suggest that acetyl-L-carnitine is significantly more effective and safe than tamoxifen in the therapy of acute and early chronic Peyronie's disease.

### Effect of coenzyme Q10 in patients with kidney diseases.

Gazdikova K, Gvozdjakova A, Kucharska J, et al. *Cas Lek Cesk* 2000;140:307-310. [Article in Slovak]

**BACKGROUND:** Coenzyme Q10 belongs to important antioxidants and it has a key role in the synthesis of adenosinetriphosphate. Its beneficial effect was proven in several diseases, e.g. in mitochondrial encephalopathy, mitochondrial myopathy, mitochondrial cardiomyopathy. **MATERIAL AND METHODS:** All 15 patients of the studied group (5 with tubulopathy and 10 with chronic tubulointerstitial nephritis) received antioxidative therapy for three months (E vitamin, C vitamin, riboflavin) and for the last two months coenzyme Q10 was added. Renal functions, spectrum of lipids, parameters of lipid peroxidation (malondialdehyde), levels of alpha-tocopherol, beta-carotene, coenzyme Q10. **RESULTS:** Before the substitutive antioxidative treatment, coenzyme Q10 levels reached in blood 0.11 +/- 0.03 mumol/l and 0.15 +/- 0.04 mumol/l in plasma. These values were well below the reference range (rr) is 0.4 +/- 1.0 mumol/l). After the substitution coenzyme Q10 levels significantly increased ( $p < 0.001$ ) to the values of 1.66 +/- 0.16 mumol/l in blood and to 1.78 +/- 0.27 mumol/l in plasma. Plasma levels of beta-carotene increased from the markedly subnormal values 0.25 +/- 0.07 mumol/l (rr > 0.8 mumol/l) to 0.56 +/- 0.02 mumol/l (no statistical difference). Plasma levels of alpha-tocopherol remained within the reference range 32.15 +/- 4.73 mumol/l (rr 15-30 mumol/l) and they increased up to the plasma level of 44.83 +/- 5.82 mumol/l during the period of testing. Malondialdehyde levels did not significantly change within the testing period. No changes in renal functions and parameters of lipid metabolism were described. Patients well tolerated the treatment and no adverse effects were seen during the period of observation. **CONCLUSIONS:** Our results ascertained that levels of antioxidant CoQ10 were lower in patients with nephropathy who underwent conservative treatment with peroral substitution. Such deficit can be amended by CoQ10 administration, which could be therefore taken as complementary treatment of nephrology.

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### **Glycyrrhizin-induced reduction of ALT in European patients with chronic hepatitis C.**

van Rossum TG, Vulto AG, Hop WC, Schalm SW. *Am J Gastroenterol* 2001;96:2432-2437.

**OBJECTIVE:** In Japan, ALT normalization induced by long-term i.v. glycyrrhizin treatment reportedly reduces the progression of liver disease to hepatocellular carcinoma in chronic hepatitis C patients. The aim of this study was to evaluate the short-term (4-wk) feasibility and efficacy on serum ALT of three or six times per week i.v. glycyrrhizin therapy in European patients. **METHODS:** Patients with chronic hepatitis C, nonresponders, or unlikely to respond (genotype 1/cirrhosis) to interferon therapy were included in this study. Medication was administered i.v. three or six times per week for 4 wk; follow-up also lasted 4 wk. **RESULTS:** Sixty-nine out of 72 treatment courses were completed according to protocol. There were no significant changes in ALT levels within the placebo group (n = 13). The mean percentage ALT decrease from baseline at the end of treatment was 26% and 47% for the three times per week and six times per week treatment group, respectively (both p < 0.001 vs placebo). At the end of active treatment, 10% (four of 41) and 20% (three of 15) of the patients reached normal ALT levels for the three times per week and six times per week treatment group, respectively. The ALT lowering effect disappeared after cessation of treatment. No major side effects were observed. **CONCLUSION:** It appeared feasible to treat European outpatients with chronic hepatitis C three or six times per week with i.v. glycyrrhizin. Glycyrrhizin treatment induces a significant ALT decrease in patients with chronic hepatitis C. Six times per week treatment appears more effective than three times per week.

### **Potential antioxidant effects of zinc and chromium supplementation in people with type 2 diabetes mellitus.**

Anderson RA, Roussel AM, Zouari N, et al. *J Am Coll Nutr* 2001;20:212-218.

**OBJECTIVE:** To determine the effects of combined zinc (Zn) and chromium (Cr) supplementation on oxidative stress and glucose homeostasis of people with type 2 diabetes. **DESIGN:** Tunisian adult subjects with HbA1C > 7.5% were supplemented for 6 months with 30 mg/d of Zn as Zn gluconate or 400 microg/d of Cr as Cr picolinate or combined Zn/Cr supplementation or placebo. The effects of supplementation on plasma zinc (Zn), copper (Cu), selenium (Se), urinary Zn, Cr, plasma thiobarbituric acid reactive substances (TBARS), Cu-Zn superoxide dismutase (SOD) and Se glutathione peroxidase (GPx) in red blood cells, blood lipids and lipoproteins, HbA1C and fasting glucose were measured at the beginning of the study and after six months. **RESULTS:** At the beginning of the study, more than 30% of the subjects may have been Zn deficient with plasma Zn values less than 10.7 micromol/L, whereas levels of plasma Cu, Se and antioxidant RBC enzyme activities were in the normal ranges. Following supplementation, there were significant decreases of plasma TBARS in the Cr (13.6%), Zn (13.6%) and Zn/Cr (18.2%) groups with no significant changes in the placebo group. The value for the TBARS of the control healthy Tunisian subjects was 2.08 +/- 0.04 micromol/L and that of the Tunisian subjects with diabetes was 3.32 +/- 0.05 micromol/L. This difference of 1.24 micromol/L between the control group and the subjects with diabetes was reduced from 36% to 50% in the three supplemented groups. Supplementation did not modify significantly HbA1C nor glucose homeostasis. No adverse effects of Zn supplementation were observed on Cu status. HDL cholesterol nor interactions in Zn or Cr. **CONCLUSIONS:** These data suggest the potential beneficial antioxidant effects of the individual and combined supplementation of Zn and Cr in people with type 2 DM. These results are particularly important in light of the deleterious consequences of oxidative stress in people with diabetes.

### **Is eradication of *Helicobacter pylori* with colloidal bismuth subcitrate quadruple therapy safe?**

Phillips RH, Whitehead MW, Doig LA. *Helicobacter* 2001;6:151-156.

**BACKGROUND:** When standard triple therapy fails to eradicate *Helicobacter pylori*, quadruple 'rescue' therapy is often used which, in Europe, generally comprises colloidal bismuth subcitrate (CBS) based triple therapy and a proton pump inhibitor. Since hypochlorhydria could greatly increase absorption of the toxic bismuth ion from CBS, we investigated the bismuth status of patients receiving anti-*H. pylori* quadruple therapy. **MATERIALS AND METHODS:** In a prospective open label study 34 patients with nonulcer dyspepsia or peptic ulcer disease, who had failed to eradicate *H. pylori* with standard triple therapy, were subsequently treated with CBS, omeprazole, amoxicillin and metronidazole (BOAM). A further 35 patients received triple therapy for the eradication of *H. pylori*: CBS, amoxicillin and metronidazole (BAM) (n = 18); placebo bismuth, amoxicillin and metronidazole (AM) (n = 9); or omeprazole, amoxicillin and metronidazole (OAM) (n = 8). Whole blood bismuth levels were determined before and within 24 hours of completing treatment. Analysis of bismuth was by inductively coupled plasma mass spectrometry, and concentrations were compared between groups and with the Hillemand 'alarm level' for blood bismuth (50-100 microg/l). **RESULTS:** BOAM gave higher blood bismuth levels than BAM (difference in means 13.1, CI 6.0-20.2, p <.001); three (8.8%) patients taking BOAM had concentrations within the Hillemand alarm level at 54.2, 64.7 and 91.8 microg/l. OAM and AM did not alter baseline blood bismuth levels. **CONCLUSIONS:** Caution should be observed in prescribing CBS with gastric acid suppression, and alternative bismuth preparations should be considered.

### **Serum melatonin circadian profile in women suffering from the genital tract cancers.**

Karasek M, Kowalski AJ, Zylinska K.  
*Neuroendocrinol Lett*  
2000;21:109-113.

**OBJECTIVES:** Although there is increasing evidence that the pineal gland may play a role in human malignancy, the studies on melatonin concentrations in different types of malignant tumors brought about controversial results. However, changes in melatonin concentrations have been observed in some types of human malignant tumors. Therefore we decided to study the circadian melatonin rhythm in patients suffering from malignant tumors of the female genital tract, and to compare them with subjects free from neoplastic disease (healthy volunteers and patients with myomatous uterus). **MATERIAL AND METHODS:** A total of 46 women were analyzed in this study. The subjects were divided into 3 groups. The first group consisted of 23 patients with malignant tumors of the genital tract (mean age 50.3 $\pm$ 2.2 years; mean $\pm$ -SEM, range 32-77 years). The second group consisted of 16 healthy volunteers (mean age 50.9 $\pm$ 1.8 years; mean $\pm$ -SEM, range 42-63) who served as the first control group, whereas the third group consisted of 7 subjects who suffered from myomatous uterus (mean age 45.7 $\pm$ 2.3 years; mean $\pm$ -SEM, range 39-56) and served as the second control group without malignancy. Blood samples were collected at 08:00, 12:00, 16:00, 20:00, 22:00, 24:00, 02:00, 04:00, 06:00 and 08:00 h. Melatonin concentration was measured using RIA kit. **RESULTS:** There were no significant differences in circadian melatonin profiles among the three groups studied. Taking into consideration the type of tumor of the genital tract, significantly lower melatonin secretion has been found in patients with endometrial cancer in comparison with tumor-free control groups, whereas no significant differences in melatonin secretion have been observed between tumor-free control groups and patients with invasive ovarian cancer and squamous cervical cancer. However, significant differences have been observed between endometrial cancer and invasive ovarian cancer. **CONCLUSION:** It seems probable that melatonin concentrations in human malignancy may, at least partly, depend on hormone dependency of the particular type of tumor.

# Abstracts

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## Recently Published Abstracts

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### **Efficacy and tolerability of a standardized willow bark extract in patients with osteoarthritis: randomized placebo-controlled, double blind clinical trial.**

Schmid B, Ludtke R,  
Selbmann HK, et al.

*Phytother Res* 2001;15:344-350.

This study assessed the clinical efficacy of a chemically standardized willow bark extract in the treatment of osteoarthritis. Willow bark extract, in a dose corresponding to 240 mg salicin/day, was compared with placebo in a 2-week, double-blind, randomized controlled trial. The primary outcome measure was the pain dimension of the WOMAC Osteoarthritis Index. Secondary outcome measures included the stiffness and physical function dimensions of the WOMAC, daily visual analogue scales (VAS) on pain and physical function, and final overall assessments by both patients and investigators. A total of 78 patients (39 willow bark extract, 39 placebo) participated in the trial. A statistically significant difference between the active treatment and the placebo group was observed in the WOMAC pain dimension ( $d = 6.5$  mm, 95% C.I. = 0.2-12.7 mm,  $p = 0.047$ ); the WOMAC pain score was reduced by 14% from the baseline level after 2 weeks of active treatment, compared with an increase of 2% in the placebo group. The patient diary VAS confirmed this result, and likewise the final overall assessments showed superiority of the willow bark extract over the placebo (patients' assessment,  $p = 0.0002$ ; investigators' assessment,  $p = 0.0073$ ). It is concluded that the willow bark extract showed a moderate analgesic effect in osteoarthritis and appeared to be well tolerated.

### **Rice bran oil and gamma-oryzanol in the treatment of hyperlipoproteinaemias and other conditions.**

Cicero AF, Gaddi A.

*Phytother Res* 2001;15:277-289.

Diet is the first (and sometimes the only) therapeutic approach to hyperlipoproteinaemias. Rice bran oil and its main components (unsaturated fatty acids, triterpene alcohols, phytosterols, tocotrienols, alpha-tocopherol) have demonstrated an ability to improve the plasma lipid pattern of rodents, rabbits, non-human primates and humans, reducing total plasma cholesterol and triglyceride concentration and increasing the high density lipoprotein cholesterol level. Other potential properties of rice bran oil and gamma-oryzanol, studied both in vitro and in animal models, include modulation of pituitary secretion, inhibition of gastric acid secretion, antioxidant action and inhibition of platelet aggregation. This paper reviews the available data on the pharmacology and toxicology of rice bran oil and its main components with particular attention to those studies relating to plasma lipid altering effects.

**Topical progesterone cream has antiproliferative effect on estrogen-stimulated endometrium.**

Anasti JN, Leonetti HB, Wilson KJ. *Obstet Gynecol* 2001;97:S10.

Objective: Transdermal progesterone cream (PC) has become a popular alternative to hormone replacement therapy despite the lack of control trials. We designed a study to determine the effect of topical PC on the estrogen-stimulated endometrium of postmenopausal women. Method: Healthy postmenopausal women underwent an initial EMB after 14 days of oral estrogens only (0.625 mg conjugated equine estrogen [CEE]). Subjects then were randomized to 4 weeks of daily CEE with twice-daily application of vaginal or topical PC in various concentrations (placebo, 1.5%, 4%). A final EMB was performed after the 4 weeks of CEE and PC treatment. The EMBs were scored as to the degree of proliferation (EPS). The pretreatment and posttreatment EPS then were compared by ANOVA of ranks. Results: Fifty-eight women finished the study. The average age was 55.2 years, body mass index (BMI) was 26.7 kg/m<sup>2</sup>, and years since menopause was 6.2. All routes and concentrations of PC resulted in significant decrease in EPS from pretreatment and posttreatment EMB (P <0.05). Both topical and vaginal placebo groups showed no difference in their EPS pretreatment and posttreatment EMB. Aversion to the application of PC was 35 % in the vaginal group versus 0% in the topical group. Conclusion: Topical and vaginal application of progesterone cream appears to have an antiproliferative effect on the endometrium. Patients preferred the topical application of progesterone cream

# Abstracts

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## Recently Published Abstracts

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### **Oral succimer decreases the gastrointestinal absorption of lead in juvenile monkeys.**

Cremin JD Jr, Luck ML, Laughlin NK, Smith DR.  
*Environ Health Perspect*  
2001;109:613-619.

Although succimer (Chemet, meso-2,3-dimercaptosuccinic acid, DMSA) is considered to be a safe and effective chelating agent for the treatment of lead poisoning in humans, there is concern that it may increase the gastrointestinal (GI) absorption and retention of Pb from exposures suffered concurrent with treatment. This concern is justified because the availability of Pb-safe housing during outpatient treatment with oral succimer is limited. We used a juvenile nonhuman primate model of moderate childhood Pb intoxication and a sensitive double stable Pb isotope tracer methodology to determine whether oral succimer chelation affects the GI absorption and whole-body retention of Pb. Infant rhesus monkeys (n = 17) were exposed to Pb daily for 1 year postpartum to reach and maintain a target blood lead (BPb) level of 35-40 microg/dL. Animals were administered succimer (n = 9) or vehicle (n = 8) over two successive 19 day succimer treatment regimens beginning at 53 and 65 weeks of age. The present study was conducted over the second chelation regimen only. Animals received a single intravenous (iv) dose of stable (204)Pb tracer (5 microg, 24.5 nmol) followed by a single oral dose of stable (206)Pb tracer (72.6 microg, 352 nmol) immediately before chelation, in order to specifically evaluate GI Pb absorption and whole-body Pb retention with treatment. We collected complete urine and fecal samples over the first 5 days and whole blood over the first 8 days of treatment for analyses of stable Pb isotopes using magnetic sector inductively-coupled plasma mass spectrometry. Results indicate that succimer significantly reduced the GI absorption of Pb (vehicle, 64.9% +/- 5.5; succimer, 37.0% +/- 5.8; mean +/- SEM). Succimer also significantly increased the urinary excretion of endogenous Pb by approximately 4-fold over the vehicle treatment, while endogenous fecal Pb excretion was decreased by approximately 33%. Finally, although succimer reduced the whole-body retention of endogenous Pb by approximately 10% compared to vehicle, the majority (77%) of the administered internal dose of Pb tracer was retained in the body when assessed after 5 days of treatment. These data do not support the concern that succimer treatment increases GI Pb absorption.

**The effects of treatment with alpha-lipoic acid or evening primrose oil on vascular hemostatic and lipid risk factors, blood flow, and peripheral nerve conduction in the streptozotocin-diabetic rat.**

Ford I, Cotter MA, Cameron NE, Greaves M. *Metabolism* 2001;50:868-875.

Oxidative stress and defective fatty acid metabolism in diabetes may lead to impaired nerve perfusion and contribute to the development of peripheral neuropathy. We studied the effects of 2-week treatments with evening primrose oil (EPO; n = 16) or the antioxidant alpha-lipoic acid (ALA; n = 16) on endoneurial blood flow, nerve conduction parameters, lipids, coagulation, and endothelial factors, in rats with streptozotocin-induced diabetes. Compared with their nondiabetic littermates, untreated diabetic rats had impaired sciatic motor and saphenous sensory nerve-conduction velocity (NCV;  $P < .001$ ), reduced endoneurial blood flow ( $P < .001$ ), and increased serum triglycerides ( $P < .01$ ), cholesterol ( $P < 0.01$ ), plasma factor VII ( $P < .0001$ ), and von Willebrand factor (vWF;  $P < .0001$ ). Plasma fibrinogen and serum high-density lipoprotein concentrations were not significantly different. Treatment with either ALA or EPO effectively corrected the deficits in NCV and endoneurial blood flow. ALA was associated with marked and statistically significant decreases in fibrinogen, factor VII, vWF, and triglycerides ( $P < .01$ , paired t tests before v after treatment). In contrast, EPO was associated with significant ( $P < .05$ ) increases in fibrinogen, factor VII, vWF, triglycerides, and cholesterol and a significant decrease in high-density lipoprotein. Changes in levels of coagulation factors and lipids, qualitatively similar to those found with EPO, were obtained with a diet containing sunflower oil (to control for caloric and lipid content) or with a normal diet alone. Blood glucose and hematocrit levels were not significantly altered by treatments. These data suggest that although both ALA and EPO improve blood flow and nerve function, their actions on vascular factors differ. The marked effects of ALA in lowering lipid and hemostatic risk factors for cardiovascular disease indicate potential antithrombotic and antiatherosclerotic actions that could be of benefit in human diabetes and merit further study.

# Abstracts

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## Recently Published Abstracts

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### **Exposure to soy-based formula in infancy and endocrinological and reproductive outcomes in young adulthood.**

Strom BL, Schinnar R, Ziegler EE, et al. *JAMA* 2001;286:807-814.

**CONTEXT:** A large body of evidence documents the role of phytoestrogens in influencing hormone-dependent states. Infants fed soy formula receive high levels of phytoestrogens, in the form of soy isoflavones, during a stage of development at which permanent effects are theoretically possible. However, a paucity of data exists on the long-term effects of infant soy formulas. **OBJECTIVE:** To examine the association between infant exposure to soy formula and health in young adulthood, with an emphasis on reproductive health. **DESIGN, SETTING, AND PARTICIPANTS:** Retrospective cohort study conducted from March to August 1999 among adults aged 20 to 34 years who, as infants, participated during 1965-1978 in controlled feeding studies conducted at the University of Iowa, Iowa City (248 were fed soy formula and 563 were fed cow milk formula during infancy). **MAIN OUTCOME MEASURES:** Self-reported pubertal maturation, menstrual and reproductive history, height and usual weight, and current health, compared based on type of formula exposure during infancy. **RESULTS:** No statistically significant differences were observed between groups in either women or men for more than 30 outcomes. However, women who had been fed soy formula reported slightly longer duration of menstrual bleeding (adjusted mean difference, 0.37 days; 95% confidence interval [CI], 0.06-0.68), with no difference in severity of menstrual flow. They also reported greater discomfort with menstruation (unadjusted relative risk for extreme discomfort vs no or mild pain, 1.77; 95% CI, 1.04-3.00). **CONCLUSIONS:** Exposure to soy formula does not appear to lead to different general health or reproductive outcomes than exposure to cow milk formula. Although the few positive findings should be explored in future studies, our findings are reassuring about the safety of infant soy formula.

**Different isoforms of tocopherols enhance nitric oxide synthase phosphorylation and inhibit human platelet aggregation and lipid peroxidation: implications in therapy with vitamin E.**

Li D, Saldeen T, Romeo F, Mehta JL. *J Cardiovasc Pharmacol Ther* 2001;6:155-161.

Background: alpha-Tocopherol has received much attention in the primary and secondary prevention of coronary artery disease. Absence of other isoforms, such as gamma- and delta-tocopherol, in commercial preparations of vitamin E may account for the inconsistent results of clinical trials. Since platelet aggregation is intimately involved in thrombogenesis, the relative effects of alpha-, gamma-, and delta-tocopherol and their combination were examined on human platelet aggregation, lipid peroxidation, and constitutive nitric oxide synthase (cNOS) activity. Methods and Results: Human platelets were incubated with the three different isoforms of tocopherol and their combination for 30 minutes, and then ADP-induced platelet aggregation measured. All three isoforms of tocopherol markedly and similarly decreased platelet aggregation in a concentration (120-480 microM)-dependent manner. All three tocopherols also decreased the level of the lipid peroxidation product, malondialdehyde (MDA), and increased NO release ( $P < 0.05$  vs control). These isoforms of tocopherol did not affect cNOS protein expression, but enhanced cNOS phosphorylation in platelets. The combination of three tocopherols in a concentration found in nature was more potent than alpha-, gamma-, or delta-tocopherol alone in this regard. Conclusion: These observations suggest that all three major isoforms of tocopherol have a similar effect on human platelet aggregation. The three isoforms appear to attenuate platelet aggregation at least in part via a decrease in free radical generation and an increase in platelet cNOS activity. The combination of tocopherols has a synergistic platelet inhibitory effect. Future clinical trials should concentrate on the combination of these three isoforms of tocopherols.

### **Herbal medicines and perioperative care.**

Ang-Lee MK, Moss J, Yuan CS. *JAMA* 2001;286:208-216.

**CONTEXT:** Widespread use of herbal medications among the presurgical population may have a negative impact on perioperative patient care. **OBJECTIVES:** To review the literature on commonly used herbal medications in the context of the perioperative period and provide rational strategies for managing their preoperative use. **DATA SOURCES:** The MEDLINE and Cochrane Collaboration databases were searched for articles published between January 1966 and December 2000 using the search terms herbal medicine, phytotherapy, and alternative medicine and the names of the 16 most commonly used herbal medications. Additional data sources were obtained from manual searches of recent journal articles and textbooks. **STUDY SELECTION:** We selected studies, case reports, and reviews addressing the safety and pharmacology of 8 commonly used herbal medications for which safety information pertinent to the perioperative period was available. **DATA EXTRACTION:** We extracted safety, pharmacodynamic, and pharmacokinetic information from the selected literature and reached consensus about any discrepancies. **DATA SYNTHESIS:** Echinacea, ephedra, garlic, ginkgo, ginseng, kava, St John's wort, and valerian are commonly used herbal medications that may pose a concern during the perioperative period. Complications can arise from these herbs' direct and pharmacodynamic or pharmacokinetic effects. Direct effects include bleeding from garlic, ginkgo, and ginseng; cardiovascular instability from ephedra; and hypoglycemia from ginseng. Pharmacodynamic herb-drug interactions include potentiation of the sedative effect of anesthetics by kava and valerian. Pharmacokinetic herb-drug interactions include increased metabolism of many drugs used in the perioperative period by St John's wort. **CONCLUSIONS:** During the preoperative evaluation, physicians should explicitly elicit and document a history of herbal medication use. Physicians should be familiar with the potential perioperative effects of the commonly used herbal medications to prevent, recognize, and treat potentially serious problems associated with their use and discontinuation.