**Selected by
Reinhard Saller
Zürich**

Latest Publications You Should Not Miss

Gertsch J: Botanical drugs, synergy, and network pharmacology: Forth and back to intelligent mixtures. *Planta Med* 2011;77:1086–1098.

For centuries the science of pharmacognosy has dominated rational drug development until it was gradually substituted by target-based drug discovery in the last fifty years. Pharmacognosy stems from the different systems of traditional herbal medicine and its ‘reverse pharmacology’ approach has led to the discovery of numerous pharmacologically active molecules and drug leads for humankind. But do botanical drugs also provide effective mixtures? Nature has evolved distinct strategies to modulate biological processes, either by selectively targeting biological macromolecules or by creating molecular promiscuity or polypharmacology (one molecule binds to different targets). Widely claimed to be superior over monosubstances, mixtures of bioactive compounds in botanical drugs allegedly exert synergistic therapeutic effects. Despite evolutionary clues to molecular synergism in nature, sound experimental data are still widely lacking to support this assumption. In this short review, the emerging concept of network pharmacology is highlighted, and the importance of studying ligand-target networks for botanical drugs is emphasized. Furthermore, problems associated with studying mixtures of molecules with distinctly different pharmacodynamic properties are addressed. It is concluded that a better understanding of the polypharmacology and potential network pharmacology of botanical drugs is fundamental in the ongoing rationalization of phytotherapy.

Zeng Y, Song JX, Shen XC: Herbal remedies supply a novel prospect for the treatment of atherosclerosis: A review of current mechanism studies. *Phytother Res* 2012;26:159–167.

Atherosclerosis (AS) is a systemic cardiovascular disease with complicated pathogenesis involving oxidative stress, endothelial dysfunction and chronic inflammation. Increasing lines of evidence have questioned the statins-dominated treatment for AS, including their dangerous side-effects

such as the breakdown of muscle when taken in larger doses. A multi-faceted approach that addresses all major risk factors or pathological targets may provide an ideal treatment for AS. Studies of the herbal remedies on the prevention and treatment of AS have received much attention in recent years. This review summarizes some important experimental findings regarding their mechanisms of action on AS. Using the pre-set PUBMED searching syntax and inclusion criteria, representative citations published in English concerning the experimental studies of 14 herbal materials were included. We found that many extracts and (or) single compounds from these herbal materials, such as *Salvia miltiorrhiza*, *Curcuma longa*, *Rheum undulatum* and *Panax notoginseng*, could regulate multiple key targets involved in the initiation and propagation of AS. Some important findings about the effects of herbal formulations on AS were also reviewed. Given the complicated nature of AS and the holistic, combinational approach of herbal remedies, we propose that mixed herbal preparations with multiple active ingredients may be preferable for the prevention and treatment of AS. Further rigorously designed pharmacological evaluation and multi-centred clinical trials are warranted.

Risoldi Cochrane Z, Gregory P, Wilson A: Quality of natural product clinical trials: A comparison of those published in alternative medicine versus conventional medicine journals. *J Diet Suppl* 2011;8:135–143.

Objective: To compare the quality of natural product clinical trials published in alternative medicine journals versus those published in conventional medicine journals.

Design: Systematic search and review of the literature. Randomized controlled trials of natural products were included if they were published in English between 2003 and 2008. Articles were categorized by their journal of publication (alternative medicine versus conventional medicine). Two independent reviewers evaluated study quality using guidelines from the Cochrane Collaboration. The results with respect to the primary outcome (positive or negative) were also assessed.

Results: Thirty articles were evaluated, 15 published in alternative medicine journals and 15 in conventional medicine journals. Of articles pub-

lished in alternative medicine journals, 33.33% (n = 5) were considered low quality, and none were considered high quality. Of articles published in conventional medicine journals, 26.67% (n = 4) were considered low quality and 6.67% (n = 1) were considered high quality. Two thirds of all trials reviewed were of unclear quality, due to inadequate reporting of information relating to the study's methodology. Similar proportions of positive and negative primary outcomes were found in alternative and conventional medicine journals, and low-quality articles were not more likely to report a positive primary outcome (Fisher's exact test, two-tailed $p = 287$).

Conclusion: The quality of natural product randomized controlled trials was similar among alternative and conventional medicine journals. Efforts should be made to improve the reporting of natural product clinical trials for accurate determinations of study quality to be possible.

Efferth T, Koch E: Complex interactions between phytochemicals. The multi-target therapeutic concept of phytotherapy. Curr Drug Targets 2011;12:122-132.

Drugs derived from natural resources represent a significant segment of the pharmaceutical market as compared to randomly synthesized compounds. It is a goal of drug development programs to design selective ligands that act on single disease targets to obtain highly effective and safe drugs with low side effects. Although this strategy was successful for many new therapies, there is a marked decline in the number of new drugs introduced into clinical practice over the past decades. One reason for this failure may be due to the fact that the pathogenesis of many diseases is rather multi-factorial in nature and not due to a single cause. Phytotherapy, whose therapeutic efficacy is based on the combined action of a mixture of constituents, offers new treatment opportunities. Because of their biological defence function, plant secondary metabolites act by targeting and disrupting the cell membrane, by binding and inhibiting specific proteins or they adhere to or intercalate into RNA or DNA. Phytotherapeutics may exhibit pharmacological effects by the synergistic or antagonistic interaction of many phytochemicals. Mechanistic reasons for interactions are bioavailability, interference with cellular transport processes, activation of pro-drugs or deactivation of active compounds to inactive metabolites, action of synergistic partners at different points of the same signalling cascade (multi-target effects) or inhibition of binding to target proteins. 'Omics' technologies and systems biology may facilitate unravelling synergistic effects of herbal mixtures.

Kim HG, Oh MS: Herbal medicines for the prevention and treatment of Alzheimer's disease. Curr Pharm Des 2012;18:57-75.

Alzheimer's disease (AD) is a chronic neurodegenerative disorder and is the most common cause of progressive dementia in aging. Research on AD therapy has been partly successful in terms of developing symptomatic treatments, but there have been a number of failures with regard to developing disease-modifying therapies. The pathogenesis of AD remains unclear and the present one-drug, one-target paradigm for anti-AD treatment appears to be clinically unsuccessful. In many countries, traditional herbal medicines are used to prevent or treat neurodegenerative disorders, and some have been developed as nutraceuticals or functional foods. This review briefly introduces progress in the development of anti-AD treatments and then focuses on recent advances in the research, characteristics, and development of herbal medicines. Because AD arises via multiple pathological or neurotoxic pathways, herbal medicines have the potential to be developed into optimum pharmaceuticals and nutraceuticals for AD because of their multi-function, multi-target characteristics.

Bakhshaei M, Jabbari F, Hoseini S, Farid R, Sadeghian MH, Rajati M, Mohamadpoor AH, Movahhed R, Zamani MA: Effect of silymarin in the treatment of allergic rhinitis. Otolaryngol Head Neck Surg 2011;145:904-909.

Objective: Although the role of oxidative stresses has been confirmed in the pathophysiology of allergic rhinitis and the protective effect of silymarin against oxidative stresses has been proven in different organs, no study has yet been conducted on the impact of silymarin on allergic rhinitis treatment.

Study design: A randomized clinical trial study.

Setting: Two tertiary referral centers with otorhinolaryngology-head and neck surgery and allergy and immunology departments.

Patients and methods: In a randomized clinical trial, 94 patients with the signs and symptoms of allergic rhinitis and a positive skin prick test were selected and randomly divided into 2 groups. Their signs and symptoms, eosinophil percentage on nasal smear, serum IgE, and interleukin (IL-4, IL-5, interferon- γ) levels were recorded. The study group was treated with silymarin, whereas the control group received placebo, both for 1 month, along with routine antihistamine treatment. At the end of the treatment course, clinical and laboratory findings were statistically analyzed.

Results: Sixty patients completed the trial. Based on the Sino-Nasal Outcome Test 20 (SNOT-20), a significant improvement in clinical symptom severity was observed in both groups (9.23 ± 5.14 vs 2.20 ± 2.69 ; $P < .001$), which was statistically significantly higher in the study group ($P < .001$). Posttreatment percentage of nasal eosinophils and cytokine levels showed no significant difference ($P > .05$). Rise in serum IgE level was seen after treatment with silymarin ($P = .003$).

Conclusion: Considering the statistically effective role of silymarin in alleviating the severity of allergic rhinitis symptoms, applying this herbal antioxidant along with other medications may result in better management.

Ngan A, Conduit R: A double-blind, placebo-controlled investigation of the effects of *Passiflora incarnata* (passionflower) herbal tea on subjective sleep quality. Phytother Res 2011;25:1153-1159.

Passiflora incarnata is a traditional herbal sedative, anxiolytic and a popular sleep aid used for the treatment of sleep disturbance. Several controlled experiments have demonstrated enhanced sleep in laboratory animals, but clinical trials in humans are lacking. The aim of the present study was to investigate the efficacy of *Passiflora incarnata* herbal tea on human sleep, as measured using sleep diaries validated by polysomnography (PSG). This study featured a double-blind, placebo-controlled, repeated-measures design with a counterbalanced order of treatments (passionflower vs placebo tea), separated by a 1 week washout period. Forty-one participants (18-35 years) were exposed to each treatment for a week, whereby they consumed a cup of the tea and filled out a sleep diary for 7 days, and completed Spielbergers state-trait anxiety inventory on the seventh morning. Ten participants also underwent overnight PSG on the last night of each treatment period. Of six sleep-diary measures analysed, sleep quality showed a significantly better rating for passionflower compared with placebo ($t(40) = 2.70$, $p < 0.01$). These initial findings suggest that the consumption of a low dose of *Passiflora incarnata*, in the form of tea, yields short-term subjective sleep benefits for healthy adults with mild fluctuations in sleep quality.