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[6]-Gingerol: A Novel AT₁ Antagonist for the Treatment of Cardiovascular Disease

<https://www.thieme-connect.com/ejournals/abstract/10.1055/s-0032-1328262>
Planta Med 2013; 79(05): 322-326. by Qing Liu

Abstract:

Considering the prevalence of cardiovascular disease in public health and the limited validated therapeutic options, this study aimed to find novel compounds targeting the angiotensin II type 1 receptor, accepted as a therapeutic target in

cardiovascular disease. A small library consisting of 89 compounds from 39 Chinese herbs was profiled using a cell-based calcium mobilization assay which was developed and characterized for

high-throughput screening. [6]-Gingerol derived from *Zingiber officinale* Roscoe (ginger) was identified as a novel angiotensin II type 1 receptor antagonist, with an IC_{50} value of 8.173 μ M. The hit was further tested by a specificity assay indicating that it had no antagonistic effects

on other evaluated GPCRs, such as endothelin receptors. The major ingredient of ginger, [6]-gingerol, could inhibit angiotensin II type 1 receptor activation, which partially clarified the mechanism of ginger regulating blood pressure and strengthening heart in the cardiovascular system.

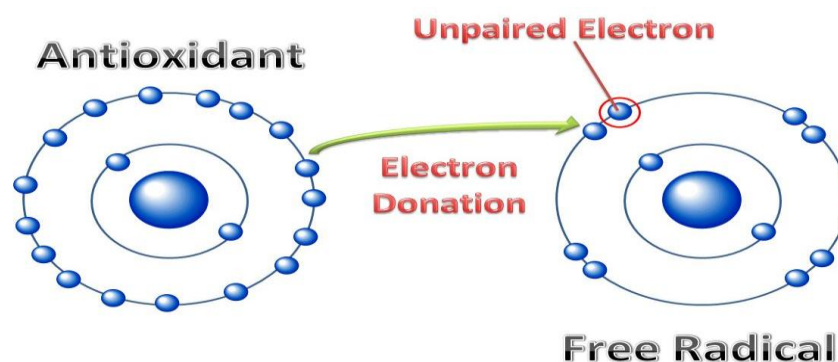
Chinese Medicinal Herbs as Source of Antioxidant Compounds - Where Tradition Meets the Future

<http://www.ingentaconnect.com/content/ben/cmc/2013/00000020/00000008/art00003>

Current Medicinal Chemistry, Volume 20, Number 8, March 2013, pp. 984-1004(21); By Matkowski, A

Medicinal plants are an essential part of Traditional Chinese Medicine (TCM), an ancient complex therapy considered today as one of the most complete complementary medicine system. Chinese Herbal Medicines (CHM) listings included in Chinese Materia Medica cover more than 1500 plants and a great number of composite preparations. Recently, several TCM herbs have been included into European Pharmacopoeia and many more are on the waiting list. The efficiency of TCM is based on the reinforcing of an organism's natural healing power and the ability to restore the energy homoeostasis. A likely mechanism of at least some of the activities is interacting with redox balance and prevention of oxidative stress. During the past two decades, hundreds of crude herbs, extracts, and isolated compounds have been screened for their antioxidant properties in vitro and in vivo.

Consequently, some of traditional Chinese herbs can be regarded as source of very efficient antioxidant compounds, and this activity could explain some of their therapeutic and preventive usefulness. In this review, we outline the recent achievements in the worldwide quest for more efficient antioxidants, with Chinese medicinal and food plants in the central point. Various classes of antioxidant compounds will be mentioned, such as polyphenols or terpenoids that can act either as direct reactive oxygen species scavengers, transition metal reducers and chelators, or as chain breaking antioxidants. Some methodological considerations will be also discussed, with emphasis on the potential importance of the results obtained with antioxidant assays for human health and disease prevention. In this context, several examples of selected, most promising Chinese medicinal plants will be also presented in more detail.



Prescription Pattern of Chinese Herbal Products for Diabetes Mellitus in Taiwan: A Population-Based Study

<http://dx.doi.org/10.1155/2013/201329>

Evidence-Based Complementary and Alternative Medicine Volume 2013 (2013), Article ID 201329, 10 pages; by Chung-Yu Huang

Background. Traditional Chinese medicine (TCM), when given as a therapy for symptom relief, has gained widespread popularity among diabetic patients. The aim of this study is to analyze the utilization of TCM among type 2 diabetic patients in Taiwan. **Methods.** The use of TCM for type 2 diabetic patients were evaluated using a randomly sampled cohort of 1,000,000 beneficiaries recruited from the National Health Insurance Research Database. **Results.** Overall, 77.9% ($n = 31,289$) of type 2 diabetic patients utilized TCM and 13.9% ($n = 4,351$) of them used TCM for the treatment of type 2 diabetes. Among the top ten most frequently

prescribed herbal formulae, four remedies, Zhi-Bo-Di-Huang-Wan, Qi-Ju-Di-Huang-Wan, Ji-Sheng-Shen-Qi-Wan and Ba-Wei-Di-Huang-Wan are derivative formulae of Liu-Wei-Di-Huang-Wan. In other words, Liu-Wei-Di-Huang-Wan and its derivatives were found to be the most common herbal formulae prescribed by TCM doctors for the treatment of diabetes in Taiwan. **Conclusion.** Although some evidence does support the use TCM to treat diabetes, the results from the current study may have been confounded by placebo effect, which emphasize the need for well conducted, double-blind, randomized, placebo-controlled studies in order to further evaluate the efficacy of Liu-Wei-Di-Huang-Wan on patients with type 2 diabetes.

Immunosuppressive Effects of the Traditional Chinese Herb Qu Mai on Human Alloreactive T Cells

<http://onlinelibrary.wiley.com/doi/10.1111/ajt.12180/abstract?deniedAccessCustomisedMessage=&userIsAuthenticated=false>

American Journal of Transplantation Volume 13, Issue 5, pages 1159-1167 May 2013-06-23.

By J. Reid-Adam

Current therapies for transplant rejection are suboptimally effective. In an effort to discover novel immunosuppressants we used cytokine ELISPOT and ELISAs to screen extracts from 53 traditional Chinese herbs for their ability to suppress human alloreactive T cells. We identified a dichloromethane-soluble fraction (Qu Mai fraction AD [QMAD]) of Qu Mai (*Dianthus superbus*) as a candidate. High-performance liquid chromatography (HPLC) analysis of QMAD revealed three dominant peaks, each with a MW ~600 Daltons and distinct from

cyclosporine and rapamycin. When we added QMAD to human mixed lymphocyte cultures, we observed dose-dependent inhibition of proliferation and IFN γ production, by naïve and memory alloreactive T cells, and observed an increased frequency of Foxp3⁺CD4⁺ T cells. To address whether QMAD induces regulatory T cells we added QMAD to anti-CD3/CD28-stimulated naïve CD4 T cells and observed a dose-dependent upregulation of Foxp3 associated with new suppressive capacity. Mechanistically, QMAD did not induce T cell IL-10 or TGF β but

blocked T cell AKT phosphorylation, a key signaling nexus required for T cell proliferation and expansion, that simultaneously prevents Foxp3 transcription. Our findings provide novel insight into the antiinflammatory effects of one



traditional Chinese herb, and support the need for continued isolation, characterization and testing of QMAD-derived components as immune suppressants for transplant rejection.



The safety and effectiveness of TM81, a Chinese herbal medicine, in the treatment of type 2 diabetes: a randomized double-blind placebo-controlled trial

<http://onlinelibrary.wiley.com/doi/10.1111/dom.12051/abstract?deniedAccessCustomisedMessage=&userIsAuthenticated=false>

Diabetes, Obesity and Metabolism. Volume 15, Issue 5, pages 448-454 May. By X. L. Tong

Aim

TM81 (or Tang-Min-Ling-Wan) is a Chinese medicine. Previous studies suggested that this medicine is effective for treating type 2 diabetes. This controlled trial evaluated the safety and effectiveness of TM81 in the treatment of type 2 diabetic patients.

Methods

This study was a large-scale controlled clinical trial to evaluate the safety and effectiveness of TM81 on type 2 diabetes. After a 2-week run-in period, 480 overweight type 2 early-stage diabetic patients [35–65 years old, HbA1c $\geq 7.0\%$, fasting plasma glucose (FPG) 7.0–13.9 mM or 2 h plasma glucose (PG) > 11.1 mM, body mass index (BMI) ≥ 24 kg/m²] were enrolled. These patients were divided into a TM81 group and placebo group in a 3:1 ratio. The subjects received 6 g TM81 or placebo, three times daily for 12 weeks.

Results:

After treatment, the HbA1c decrease was 1.02% in the TM81 group versus 0.47% in the placebo group. The FPG decreased 0.8 ± 0.1 mM in the TM81 group versus an increase of 0.2 ± 0.2 mM in the placebo group. The PG decreased 2.7 ± 0.3 mM in the TM81 group versus a decrease of 0.9 ± 0.4 mM in the placebo group (all $p < 0.05$). The TM81 was more effective for patients with higher baseline HbA1c levels. The TM81 group also showed improved β -cell function and increased homeostatic model assessment (HOMA)- β . In addition, body weight, BMI and waist circumference of subjects in the TM81 group were reduced, and the symptoms related to diabetes were improved. There were no significant differences in the types and frequency of adverse reactions between the two groups.

Conclusions:

The data showed that TM81 is effective in controlling blood glucose level and is safe to use in patients with early-stage type 2 diabetes.

Cardiovascular Protective Effects of Adjunctive Alternative Medicine (*Salvia miltiorrhiza* and *Pueraria lobata*) in High-Risk Hypertension

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3606734/>

Evid Based Complement Alternat Med. 2013; 2013: 132912. By K.S.Woo

Introduction. Hypertension in association with diabetes (DM), renal impairment (RI), and left ventricular hypertrophy (LVH) increases the risk of future cardiovascular events. We hypothesize, traditional herbal medicines Danshen and Gegen (D&G) have beneficial effects on atherogenesis in these high-risk hypertensive subjects.

Subjects and Methods. 90 asymptomatic hypertensive subjects associated with LVH (63.3%), DM (62.2%), or RI (30%) were randomized to receive D&G herbal capsules 1 gm/day, 2 gm/day, or identical placebo capsules in double-blind and parallel fashion for 12 months. Brachial flow-mediated dilation (endothelium-dependent dilation, FMD) and carotid intima-media thickness (IMT) were measured by ultrasound. All data were analyzed using the Statistical Package for Social Sciences

in Windows 16.0. **Results.** Their mean age was 55 ± 8 years, and 74.4% were male. After 12 months of adjunctive therapies and compared with baseline, there were no significant changes in blood pressure, heart rate, hematological, glucose, and creatinine profiles in both placebo and D&G groups. FMD improved significantly during D&G ($P = 0.0001$) and less so after placebo treatment ($P = 0.001$). There was a mild but significant decrease in carotid IMT after D&G ($P < 0.001$) but no significant changes after placebo. A trend of better improvement in FMD after higher versus lower D&G dosages was seen. D&G were well tolerated, with no significant adverse events or blood biochemistry changes. **Conclusion.** D&G adjunctive treatment was well tolerated and significantly improved atherogenesis in high-risk hypertensive patients, with potential in primary atherosclerosis prevention

Gegen



Danshen



Chinese Medicine Formula Lingguizhugan Decoction Improves Beta-Oxidation and Metabolism of Fatty Acid in High-Fat-Diet-Induced Rat Model of Fatty Liver Disease

<http://dx.doi.org/10.1155/2013/429738>

Evidence-Based Complementary and Alternative Medicine. Volume 2013, Article ID 429738, 9 pages by Tao Liu

Abstract

Lingguizhugan decoction (LGZG), a classic traditional Chinese medicine (TCM) formula, has been used to treat obesity and hyperlipidemia in recent years, but the related mechanisms underlying the regulation of lipid metabolism by LGZG are not clear yet. Here, we reported the effectiveness and possible mechanisms of LGZG on rats with fatty liver disease induced by high-fat diet (HFD). Our results demonstrated that LGZG significantly attenuated HFD-induced fatty liver disease, as measured by body weight, liver index, epididymal fat pad-body weight ratio (EFP/BW), liver injury, and hepatic triglycerides (TG) probably through increasing serum thyroid hormone levels, improving beta-oxidation (via modulation of TR β 1 and CPT1A expression), metabolism and transport (through modulation of SREBP-1c, ACSL and ApoB100 expression) of fatty acid. In addition, we discovered the herbal combination with the properties of warming yang to relieve water retention in the formula and proposed the biological basis of LGZG conventional effect via further study on disassembled formula. This study, for the first time, revealed the mechanisms through which LGZG regulates lipid metabolism. Furthermore, our study suggested that it might be feasible to understand the scientific implications of TCM from the perspective of classic formulas' conventional efficacy.

Anti-inflammatory effects of a Chinese herbal medicine in atherosclerosis via estrogen receptor β mediating nitric oxide production and NF- κ B suppression in endothelial cells

<http://www.nature.com/cddis/journal/v4/n3/abs/cddis201366a.html>

Cell Death and Disease (2013) 4, e551; doi:10.1038/cddis.2013.66. Published online 21 March 2013.

By L Wang

Bu-Shen-Ning-Xin Decoction (BSNXD) administration has alleviated the early pathologic damage of atherosclerosis by inhibiting the adhesion molecule expression and upregulating the estrogen receptor (ER) β expression in endothelial cells, and increasing the serum nitric oxide (NO) level without any effect on serum lipid status, endometrium and fat deposition in

liver in ovariectomized rabbits. The BSNXD-derived serum increases ER β expression in the human umbilical vein endothelial cells (HUVECs), and decreases malondialdehyde (MDA) production, and upregulates eNOS expression then increases NO synthesis through ER β -dependent pathway. NO not only suppresses the LPS-induced NF- κ B transcription in

HUVECs, but also decreases apoptosis of endothelial cells. The BSNXD-derived serum decreases monocyte chemoattractant protein-1 production, and suppresses cell adhesion molecules (ICAM-1, VCAM-1 and E-selectin) expression in HUVECs injured by oxidized low-density lipoproteins (ox-LDL), and these effects can be abolished by ER β antagonist (R,RTHC) and NO synthase inhibitor (L-NAME). The BSNXD-derived serum-treated HUVECs

supernatant reduces CCR2, LFA-1 and VLA-4 expression in monocytes cell line U937 cells, which in turn inhibits adherence of U937 to injured endothelial cells. NO synthesis increases, and MDA production decreases through ER β -mediated pathway that suppresses apoptosis and NF- κ B activity in endothelial cells that downregulates adhesion molecules expression on endothelial cells via ER β /NO/NF- κ B pathway, and in turn leukocyte adhesion, which suggests BSNXD potential value in prophylaxis atherosclerosis.

