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1. A Chinese Medicine Formula (Jinqi Jiangtang Tablet): A Review on Its Chemical Constituents, Quality Control, Pharmacokinetics Studies, Pharmacological Properties and Clinical Applications

Keywords: Clinical applications; Diabetes; Jinqi Jiangtang Tablet (JQJTT); Pharmacology; Quality control; Traditional Chinese medicine (TCM).

Yi Liu, Aiting Wang et al. *Review J Ethnopharmacol* , 236, 1-8 2019 May 23

Abstract

Ethnopharmacological relevance: Diabetes belongs to the category of "Xiao Ke Zheng" in the field of traditional Chinese medicine (TCM) and has been listed as one of the predominant diseases of TCM. Jinqi Jiangtang Tablet (JQJTT), a Chinese medicine formula composed of three herbs (Coptis chinensis, Astragalus membranaceus and Lonicera japonica), is an effective prescription for diabetes proved by randomized, double-blind, placebo-controlled trials.

Aim of the review: To analyze systematic and up-to-date classification information on the study of JQJTT, explain the problems existing in the current research of classics formulas, and further propose the solution, providing a reference for future study.

Materials and methods: Literatures on JQJTT were collected from a variety of databases, including PubMed, Google Scholar, Science Direct, Wiley, Web of Science, China National Knowledge Infrastructure, and WanFang Data. Information was also collected from books and reports, such as Chinese Pharmacopoeia, Chinese herbal classic books and reports of re-evaluation on post-marketing drugs conducted by companies.

Results: There are some problems for JQJTT: the quality control system is not perfect, the pharmacological functional mechanism is not fully explained, and clinical

applications need to be reevaluated. A few of research directions for future research are proposed: (i) the chemical quality evaluation combined with bioassay to evaluate quality; (ii) interaction based on gut microbiota in vivo; (iii) the effects of interaction between components of the polypharmacy on pharmacokinetic studies; (iv) interaction mechanism between drugs and endogenous small molecules and biomacromolecules; (v) evidence-based medicine reconfirmation for clinical evaluation.

Conclusions: The recent research status of JQJTT was summarized and analyzed from the aspects of chemical constituents, quality control, pharmacokinetics studies, pharmacological properties and clinical applications. This review takes JQJTT as an example, points out some typical problems and opinions about the TCM formulas, highlights the importance of the secondary development of classical formula, and lays a foundation for the further research.

2. Treatment of Advanced Breast Cancer with Chinese Medicinal Herbs of Fei Decoction: A Case Report

G M Lv, M Hu et al. Curr Pharm Biotechnol.14 (13), 1088-92 2014

Abstract

A 46-year-old female underwent surgery for cancer of the right breast mammary (T3N2M0) in Sep 2010. Following postsurgery, adjuvant chemotherapy of CAF regimens (cyclophosphamide+adriamycin+fluorouracil) was administered. Two years later, multiple pulmonary and skeletal metastatic lesions had been found by CT (computerized tomography) and ECT (emission computed tomograph) imaging. She received the treatment of second-line chemotherapy regimens of GP (cisplatin + gemcitabine). In the meantime, we administered Chinese traditional herb drugs (Fei Decoction, mixed a variety of effective herbal components) to help her recover from the poor condition. After taking the Chinese herbs for 2 months, the tumour marker (CEA, CA15-3) dramatically decreased, resulting in the normal range. Both lung and bone metastatic sites reduced according to CT and ECT imaging, and the patient felt free from the complaint of pulmonary and cardiac discomfort. Over time, the quality of life has been greatly improved, we have managed to prolong the PFS (progression-

free-survival) and TTP (time-to-progression) from the onset to date. CTM (Chinese traditional medicine) considers human body as a dynamic platform in which all organs are correlative and bind each other. Relationship between heart, liver, spleen, lung and kidney is like aninterlink between mother and son, and runs in cycle as a circle. In the course of this combined treatment, we showed that Chinese herbal medicine played an important role in the therapy of breast cancer. Chinese herbs might be an additional choice with their better benefits and tolerability in the treatment of recurrent breast cancer.

3. Chemical Profiles, Antioxidant Activity and Acute Toxicity of Raw and Sulfur-Fumigated Smilacis Glabrae Rhizoma

Keywords: Acute toxicity test; Antioxidant activity; Smilacis Glabrae Rhizoma; Sulfur fumigation; Ultra performance liquid chromatography

Muhua Yuan, Zhigang Yan et al. Journal of Ethnopharmacol. 234, 76-84 2019 Apr 24

Abstract

Ethnopharmacological relevance: Smilacis Glabrae Rhizoma (SGR), known as Tu-fu-ling in the China, Japan and Korea, is an herb that has been used for clearing damp and detoxification in traditional Chinese medicine for many years. The post-harvest drying of SGR has traditionally been done by the sun, but sometimes sulfur fumigation is used instead due to its low cost and high efficiency. Recent reports show that sulfur fumigation can change the chemical constitution of herbal medicines and decrease their biology activity.

Aim of the study: This study will investigate the changes to the chemical constitution, acute toxicity and antioxidant potential of SGR that occur after sulfur fumigation. To date, no studies have investigated these aspects simultaneously.

Materials and methods: An ultra-performance liquid chromatography fingerprint method was developed for analysing changes to SGR's chemical constitution caused by sulfur fumigation. The chromatography conditions were as follows: all samples were analysed on a Waters Acquity UHPLC HT3 C18 column; the linear gradient elution

was conducted with a mobile phase prepared from acetonitrile and water. All calibration curves showed good linear regression (R > 0.9991) within the tested range. The method was validated for precision, accuracy, limit of detection and quantification. Total flavonoids of the raw and sulfur-fumigated samples were also determined by ultraviolet spectrophotometry. The antioxidant properties of the extracts were evaluated using both DPPH and ABTS radical scavenging assays. The acute toxicities of the raw and sulfur-fumigated samples were investigated.

Results: The results demonstrate that the amounts of astilbin, neoastilbin, neoisoastilbin, isoastilbin, resveratrol and total flavonoids were lower in sulfur-fumigated samples than in raw samples. The antioxidant activity of the sulfur-fumigated samples was also significantly lower. Therefore, sulfur fumigation may cause chemical transformation, alter the chemical constitution, and decrease the bioactivity of SGR. Orally-administered doses did not cause mortality or changes in the general behaviour of tested mice. The LD50 was > 5000 mg/kg DW. However, the high-dose S-SGR mice had significant liver damage and high levels of plasma biochemical parameters (ALT, AST, DBIL, TBIL).

Conclusions: The results of the current study suggest that sulfur fumigation can decrease antioxidant activity in vitro; and that orally-administrated S-SGR is unsafe at doses > 3000 mg/kg dried materia medica. Therefore, sulfur-fumigation processing should be forbidden for SGR until its efficacy and safety has been demonstrated. An alternative method of sulfur fumigation for the post-harvest processing of SGR should also be developed.

4. Full-length Transcriptome Sequencing and Methyl Jasmonate-Induced Expression Profile Analysis of Genes Related to Patchoulol Biosynthesis and Regulation in Pogostemon Cablin

Xiuzhen Chen, Junren Li et al. BMC Plant Biol . 19 (1), 266 2019 Jun 20

Keywords: Expression profile; Full-length transcriptome; MeJA; Patchoulol; Pogostemon cablin

Abstract

Background: Pogostemon cablin (Blanco) Benth. (Patchouli) is an important aromatic and medicinal plant and widely used in traditional Chinese medicine as well as in the perfume industry. Patchoulol is the primary bioactive component in P. cablin, its biosynthesis has attracted widespread interests. Previous studies have surveyed the putative genes involved in patchoulol biosynthesis using next-generation sequencing method; however, technical limitations generated by short-read sequencing restrict the yield of full-length genes. Additionally, little is known about the expression pattern of genes especially patchoulol biosynthesis related genes in response to methyl jasmonate (MeJA). Our understanding of patchoulol biosynthetic pathway still remained largely incomplete to date.

Results: In this study, we analyzed the morphological character and volatile chemical compounds of P. cablin cv. 'Zhanxiang', and 39 volatile chemical components were detected in the patchouli leaf using GC-MS, most of which were sesquiterpenes. Furthermore, high-quality RNA isolated from leaves and stems of P. cablin were used to generate the first full-length transcriptome of P. cablin using PacBio isoform sequencing (Iso-Seq). In total, 9.7 Gb clean data and 82,335 full-length UniTransModels were captured. 102 transcripts were annotated as 16 encoding enzymes involved in patchouli alcohol biosynthesis. Accorded with the uptrend of patchoulol content, the vast majority of genes related to the patchoulol biosynthesis were up-regulated after MeJA treatment, indicating that MeJA led to an increasing synthesis of patchoulol through activating the expression level of genes involved in biosynthesis pathway of patchoulol. Moreover, expression pattern analysis also revealed that transcription factors participated in JA regulation of patchoulol biosynthesis were differentially expressed.

Conclusions: The current study comprehensively reported the morphological specificity, volatile chemical compositions and transcriptome characterization of the Chinese-cultivated P. cablin cv. 'Zhanxiang', these results contribute to our better understanding of the physiological and molecular features of patchouli, especially the molecular mechanism of biosynthesis of patchoulol. Our full-length transcriptome data also provides a valuable genetic resource for further studies in patchouli.

5. Molecular Identification and Expression of Sesquiterpene Pathway Genes Responsible for Patchoulol Biosynthesis and Regulation in Pogostemon Cablin

Yun Tang, Liting Zhong et al. *Bot Stud* , 60 (1), 11 2019 Jul 2

Keywords: Patchoulol; Pathway; Pogostemon cablin; Sesquiterpene; Terpenoid biosynthesis.

Abstract

Background: Many commercially important drug and flavor compounds are secondary metabolites of terpenoid origin. Pogostemon cablin, a commercially important industrial and medicinal crop, accumulates abundant patchouli oil comprised of more than 24 unique sesquiterpene compounds, with the most abundant being patchouli alcohol.

Results: In this study, we analyzed the P. cablin transcriptome library, obtaining 74 terpenoid biosynthesis-related genes, and identified their expression patterns in leaves, stems, and flowers. These genes are members of 15 different families, and we detected all the enzymes involved in the sesquiterpenes pathway that are responsible for patchoulol biosynthesis. Sequence structure, homology, conserved domain properties, and phylogeny of certain identified genes were systematically investigated. Color complementation assay was used to verify the functional activity of the MEP pathway proteins. Exogenous hormone treatment revealed that patchoulol synthesis is induced by methyl jasmonate (MeJA). Quantitative reverse-transcription PCR analysis indicated that the MVA pathway genes (acetoacetyl-CoA thiolase, 3-hydroxy-3-methylglutaryl-coenzyme A reductase, mevalonate diphosphate decarboxylase, and farnesyl diphosphate synthase) participate in patchoulol biosynthesis and are mediated by MeJA.

Conclusions: Taken together, this is the first report of integrated analysis of P. cablin MVA and MEP pathway related genes, providing a better understanding of terpenoid and/or patchoulol biosynthesis in P. cablin, and the basis for improving patchoulol production through genetic engineering.

6. Berberine Impairs Embryonic Development in Vitro and in Vivo Through Oxidative Stress-Mediated Apoptotic Processes

Chien-Hsun Huang, Zi-Wei Huang et al. Environ Toxicol , 33 (3), 280-294 Mar 2018

Keywords: apoptosis; berberine; blastocyst; embryonic development; oxidative stress.

Abstract

Berberine, an isoquinoline alkaloid isolated from several traditional Chinese herbal medicines, has been shown to suppress growth and induce apoptosis in some tumor cell lines. However, berberine has also been reported to attenuate H2 O2 -induced oxidative injury and apoptosis. The basis for these ambiguous effects of berberine-triggering or preventing apoptosis-has not been well characterized to date. In the current investigation, we examined whether berberine exerts cytotoxic effects on mouse embryos at the blastocyst stage and affects subsequent embryonic development in vitro and in vivo. Treatment of blastocysts with berberine (2.5-10 μM) induced a significant increase in apoptosis and a corresponding decrease in trophectoderm cell number. Moreover, the implantation success rate of blastocysts pretreated with berberine was lower than that of their control counterparts. Pretreatment with berberine was also associated with increased resorption of postimplantation embryos and decreased fetal weight. In an animal model, intravenous injection of berberine (2, 4, or 6 mg/kg body weight/d) for 4 days resulted in apoptosis of blastocyst cells and early embryonic developmental injury. Berberine-induced injury of mouse blastocysts appeared to be attributable to oxidative stress-triggered intrinsic apoptotic signaling processes that impaired preimplantation and postimplantation embryonic development. Taken together, our results clearly demonstrate that berberine induces apoptosis and retards early preimplantation and postimplantation development of mouse embryos, both in vitro and in vivo.

7. Buyang Huanwu Tang (Boyang Hwano Tang) for the Treatment of Post-Stroke Fatigue: Protocol for a Systematic Review of Randomized Controlled Trials

Chul Jin, Seung-Yeon Cho et al. *Medicine (Baltimore)*. 98 (37), e17116 Sep 2019

Abstract

Background: Buyang Huanwu Tang (BHT) is a well-known herbal complex used for stroke treatment and has been used mainly during post-stroke rehabilitation in East Asia. In this review, we aim to evaluate the efficacy and safety of BHT as a treatment for post-stroke fatigue (PSF).

Methods: Eight databases will be searched for relevant studies from inception to the present date. We will include randomized controlled trials (RCTs), which assess the effect and safety of BHT for the treatment of PSF. The methodological qualities, including the risk of bias (RoB), will be evaluated using the Cochrane RoB assessment tool. After screening the studies, a meta-analysis of the RCTs will be done.

Results: This study will provide high-quality synthesis of current evidence of BHT for PSF.

Conclusion: The conclusion of our systematic review will provide evidence to judge whether BHT is an effective intervention for patients with PSF.

Ethics and dissemination: Ethical approval is not required, as this study is based on the review of published research. This review will be published in a peer-reviewed journal and disseminated both electronically and in print.

Trial registration number: PROSPERO CRD42019130178.

8. Medicinal Plants and Dementia Therapy: Herbal Hopes for Brain Aging?

Elaine Perry, Melanie-Jayne R Howes et al. CNS Neurosci Ther , 17 (6), 683-98 Dec 2011

Abstract

An escalating "epidemic" of diseases like Alzheimer's has not yet been met by effective symptomatic treatments or preventative strategies. Among a few current prescription drugs are cholinesterase inhibitors including galantamine, originating from the snowdrop. Research into ethnobotanicals for memory or cognition has burgeoned in recent years. Based on a multi-faceted review of medicinal plants or phytochemicals, including traditional uses, relevant bioactivities, psychological and clinical evidence on

efficacy and safety, this overview focuses on those for which there is promising clinical trial evidence in people with dementia, together with at least one other of these lines of supporting evidence. With respect to cognitive function, such plants reviewed include sage, Ginkgo biloba, and complex mixtures of other traditional remedies. Behavioral and psychological symptoms of dementia (BPSD) challenge carers and lead to institutionalization. Symptoms can be alleviated by some plant species (e.g., lemon balm and lavender alleviate agitation in people with dementia; St John's wort treats depression in the normal population). The ultimate goal of disease prevention is considered from the perspective of limited epidemiological and clinical trial evidence to date. The potential value of numerous plant extracts or chemicals (e.g., curcumin) with neuroprotective but as yet no clinical data are reviewed. Given intense clinical need and carer concerns, which lead to exploration of such alternatives as herbal medicines, the following research priorities are indicated: investigating botanical agents which enhance cognition in populations with mild memory impairment or at earliest disease stages, and those for BPSD in people with dementia at more advanced stages; establishing an ongoing authoritative database on herbal medicine for dementia; and further epidemiological and follow up studies of promising phytopharmaceuticals or related nutraceuticals for disease prevention.

9. Chinese Herbal Formulas and Renal Fibrosis: An Overview

Yu-Li Shen, Su-Juan Wang et al. Curr Pharm Des, 24 (24), 2774-2781 2018

Keywords: Bian-Zheng-Lun-Zhi; Chinese herbal formula; chronic kidney disease; extracellular matrix (ECM); renal fibrosis; traditional Chinese Medicine (TCM)..

Abstract

All forms of chronic kidney disease (CKD) eventually lead to renal fibrosis irrespective of its origin. It is generally characterized by an excessive accumulation and deposition of extracellular matrix (ECM) and to date, no ideal treatment has been established. Bian-Zheng-Lun-Zhi (syndrome differentiation and treatment), a classic feature of traditional Chinese Medicine (TCM), is a unique method used to diagnose and treat the pathology of a disease. Zheng (syndrome) is used to demonstrate the nature of a disease completely in an extensive and specific manner. Chinese herbal formulas are

determined according to TCM theory and this review highlights these formulas and suggests a possible mechanism for their use in the treatment of renal fibrosis.

10. Single Herbal Medicine for Diabetic Retinopathy

Hong Wei Zhang, Hongying Zhang et al. Cochrane Database Syst Rev , 12 (12), CD007939 2018 Dec 19

Abstract

Background: Diabetic retinopathy is one of the major causes of blindness and the number of cases has risen in recent years. Herbal medicine has been used to treat diabetes and its complications including diabetic retinopathy for thousands of years around the world. However, common practice is not always evidence-based. Evidence is needed to help people with diabetic retinopathy or doctors to make judicious judgements about using herbal medicine as treatment.

Objectives: To evaluate the effectiveness and harm of single herbal medicine for diabetic retinopathy.

Search methods: We searched CENTRAL, which contains the Cochrane Eyes and Vision Trials Register, MEDLINE, Embase, OpenGrey, the ISRCTN registry, ClinicalTrials.gov and the ICTRP. The date of the search was 12 June 2018. We also searched the following Chinese databases in June 2013: Chinese BioMedical Literature Database (CBM), Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), Wanfang China Dissertation Database (CDDB), Wanfang China Conference Paper Database (CCPD) and the Index to Chinese Periodical Literature.

Selection criteria: We included randomised controlled trials (RCTs) and quasi-RCTs that investigated the effects of any single herb (or extracts from a single herb) as a treatment for people with diabetic retinopathy. We considered the following comparators: placebo, no treatment, non-herbal (conventional) medicine or surgical treatment.

Data collection and analysis: Two review authors independently extracted data and assessed the risk of bias in the studies. Our prespecified outcomes were: progression

of diabetic retinopathy, visual acuity, microaneurysms and haemorrhages in the retina, blood glycated haemoglobin A1c (HbA1c) (%) and adverse effects. We performed meta-analyses using risk ratios (RR) for dichotomous outcomes and mean differences (MD) for continuous outcomes, with 95% confidence intervals (CI). We assessed the certainty of the evidence using GRADE.

Main results: We included 10 studies involving 754 participants, of which nine were conducted in China and one in Poland. In all studies, participants in both groups received conventional treatment for diabetic retinopathy which included maintaining blood glucose and lipids using medicines and keeping a stable diabetic diet. In three studies, the comparator group also received an additional potentially active comparator in the form of a vasoprotective drug. The single herbs or extracts included Ruscus extract tablet, Sanqi Tongshu capsule, tetramethylpyrazine injection, Xueshuantong injection, Puerarin injection and Xuesaitong injection. The Sanqi Tongshu capsule, Xueshuantong injection and Xuesaitong injection were all made from the extract of Radix Notoginseng (San qi) and the main ingredient was sanchinoside. The risk of bias was high in all included studies mainly due to lack of masking (blinding). None of the studies reported the primary outcome of this review, progression of retinopathy.Combined analysis of herbal interventions suggested that people who took these herbs in combination with conventional treatment may have been more likely to gain 2 or more lines of visual acuity compared to people who did not take these herbs when compared to conventional intervention alone at the end of treatment (RR 1.26, 95% CI 1.08 to 1.48; 5 trials, 541 participants; low-certainty evidence). Subgroup analyses based on the different single herbs found no evidence for different effects of different herbs, but the power of this analysis was low. One study reported Sanqi Tongshu capsule might be associated with a greater reduction in microaneurysms and haemorrhages in the retina (very low-certainty evidence). The pooled analysis of two studies on tetramethylpyrazine or Xueshuantong injection showed such herbs may have had little effect on lowering HbA1c (MD 0.00, 95% CI -0.58 to 0.58; 215 participants; low-certainty evidence).There was very low-certainty evidence on adverse events. Two studies reported minor adverse events such as uncomfortable stomach, urticaria, dizziness and headache. There was no report of observation on adverse events in the other studies.

Authors' conclusions: No conclusions could be drawn about the effect of any single herb or herbal extract on diabetic retinopathy from the current available evidence. It was difficult to exclude the placebo effect as a possible explanation for observed differences due to the lack of placebo control in the included studies. Further adequately designed trials are needed to establish the evidence.

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