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Contents

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Immunomodulatory Mechanism of Bushen Huoxue Recipe Alleviates Cyclophosphamide-Induced Diminished Ovarian Reserve in Mouse Model.

https://www.ncbi.nlm.nih.gov/pubmed/28645781
J Ethnopharmacol. 2017 Jun 20. pii: S0378-8741(16)32389-3. doi: 10.1016/j.jep.2017.06.022.
By Huang C, Song K, Ma W, Ding J, Chen Z, Zhang M

Abstract

ETHNOPHARMACOLOGICAL RELEVANCE:

Bushen Huoxue recipe (BHR) is a Chinese herbal prescription composed of ten herbs and it is widely used for the treatment of diminished ovarian reserve (DOR). This study investigates the potentially beneficial effects and underlying mechanism of BHR on a cyclophosphamide (CTX) induced model of DOR in mice.

MATERIALS AND METHODS:

Granules of BHR were first subjected to high performance liquid chromatography (HPLC) to determine the exact ingredients within the mixture. We then induced DOR in mice by injecting them with 90mg/kg of CTX. Following the single intraperitoneal injection, mice then received either saline or BHR for 21 days. To assess the effects of BHR on DOR, we examined splenic and ovarian morphology, estrous cycle duration, ovarian index, follicle number, body weight, and concentration of serum E_2 and FSH. To explore the immunological mechanism behind the effects, mouse splenocytes were isolated in order to analyze the proportion of $CD4^+$, $CD8^+$ T cells and Th1, Th17 and Treg subsets by flow cytometry. The serum levels of IFN-γ, TNF-α, IL-4, IL-17A, IL-6 and IL-10 were detected using Cytometric Bead Array (CBA). Additionally, the mRNA expression levels of T-bet, RORγt and Foxp3 were measured with quantitative real-time PCR.

RESULTS:

Our results show that following treatment with BHR in DOR mice, several measures showed significant improvement. The morphology of the ovary and spleen, estrous cycle duration, body weight, ovarian index, and serum levels of E_2 and FSH recovered to approximately normal levels and the loss of follicles at all stages was significantly attenuated. Furthermore, the elevated proportions of $CD4^+$ T cells, Th1, Th17, Treg subsets and the increased serum

levels of IFN-γ, TNF-α, IL-17A, IL-6 and IL-10 as well as the mRNA expressions of T-bet, RORγt and Foxp3 in DOR mice were significantly decreased.

CONCLUSIONS:

Our results show that BHR is a promising candidate to treat DOR mice and this beneficial effect may be mediated through the downregulation of augmented autoimmunity.

Herb-Drug Interaction between the Traditional Hepatoprotective Formulation and Sorafenib on Hepatotoxicity, Histopathology and Pharmacokinetics in Rats.

https://www.ncbi.nlm.nih.gov/pubmed/28640225
Molecules. 2017 Jun 22;22(7). pii: E1034. doi: 10.3390/molecules22071034.
By Ting CT, Cheng YY, Tsai TH

Abstract

Sorafenib has been used as a standard therapy for advanced hepatocellular carcinoma (HCC). In Asia, patients with HCC are potentially treated with the combination of sorafenib
and Chinese herbal medicines to improve the efficiency and reduce the side effects of sorafenib. However, limited information about the herb-drug interactions is available. We hypothesize that the Chinese herbal medicine may exert hepatoprotective effects on the sorafenib-treated group. The aim of this study is to investigate the pharmacokinetic mechanism of drug-drug interactions of sorafenib including interacting with hepatoprotective formulation, Long-Dan-Xie-Gan-Tang formulation (LDXGT) and with two cytochrome P450 3A4 (CYP3A4) inhibitors, grapefruit juice and ketoconazole. Liver enzyme levels and histopathology of liver slices were used to evaluate sorafenib-induced hepatotoxicity and the potential hepatoprotective effects of the LDXGT formulation on subjects treated with the combination of sorafenib and the herbal medicine. In this study, a validated HPLC-photodiode array analytical system was developed for the pharmacokinetic study of sorafenib in rats. As the result of the pharmacokinetic data, pretreatment with the LDXGT formulation did not significantly interact with sorafenib compared with sorafenib oral administration alone. Furthermore,

grapefruit juice and ketoconazole did not significantly affect sorafenib metabolism. Furthermore, pretreatment with variable, single or repeat doses of the LDXGT formulation did not suppress or exacerbate the sorafenib-induced hepatotoxicity and histopathological alterations. According to these results, the LDXGT formulation is safe, but has no beneficial effects on sorafenib-induced hepatotoxicity. A detailed clinical trial should be performed to further evaluate the efficacy or adverse effects of the LDXGT formulation in combination with sorafenib in humans.

Herbal Medicine AC591 Prevents Oxaliplatin-Induced Peripheral Neuropathy in Animal Model and Cancer Patients.

https://www.ncbi.nlm.nih.gov/pubmed/28638341
Front Pharmacol. 2017 Jun 7;8:344. doi: 10.3389/fphar.2017.00344.
By Cheng X, Huo J, Wang D, Cai X, Sun X, Lu W, Yang Y, Hu C, Wang X, Cao P

Abstract

Oxaliplatin is clinically compelling because of severe peripheral neuropathy. The side effect can result in dosage reductions or even cessation of chemotherapy, and no effective treatments are available. AC591 is a standardized extract of Huangqi Guizhi Wuwu decoction, an herbal formula recorded in "Synopsis of the Golden Chamber" for improving limb numbness and pain. In this study, we investigated whether AC591 could protect against oxaliplatin-induced peripheral neuropathy. To clarify it, a rat model of oxaliplatin-induced peripheral neuropathy was established, and neuroprotective effect of AC591 was studied. Our results showed that pretreatment with AC591 reduced oxaliplatin-induced cold hyperalgesia, mechanical allodynia as well as morphological damage of dorsal root ganglion. Microarray analysis indicated the neuroprotective action of AC591 depended on the modulation of multiple molecular targets and pathways involved in the downregulation of inflammation and immune response. Moreover, AC591 enhanced the antitumor activity of oxaliplatin to some extent in Balb/c mice bearing CT-26 carcinoma cells. The efficacy of AC591 is also investigated in 72 colorectal cancer patients. After four cycles of treatment, the percentage of grades 1-2 neurotoxicity in AC591-treated group (n = 36) was 25%, whereas in the control group the incidence was 55.55% ($P < 0.01$) (n = 36). No significant differences in the tumor response rate between the two groups were found. These evidences suggested that AC591 can

prevent oxaliplatin-induced neuropathy without reducing its antitumor activity, and may be a promising adjuvant to alleviate sensory symptoms in clinical practice.

Therapeutic Potential of Baicalein in Alzheimer's Disease and Parkinson's Disease.

https://www.ncbi.nlm.nih.gov/pubmed/28634902
CNS Drugs. 2017 Jun 20. doi: 10.1007/s40263-017-0451-y.
By Li Y, Zhao J, Hölscher C.

Abstract

Alzheimer's disease and Parkinson's disease are the two most common, progressive central neurodegenerative diseases affecting the population over the age of 60 years. Apart from treatments that temporarily improve symptoms, there is no medicine currently available to inhibit or reverse the progression of Alzheimer's disease and Parkinson's disease. In traditional Chinese medicine, the root of Scutellaria baicalensis Georgi is a classic compatible component in the decoction of herbal medicine used for treating central nervous system diseases. Modern pharmacokinetic studies have confirmed that baicalein (5,6,7-trihydroxyflavone) is a major bioactive flavone constituent root of S. baicalensis Georgi. Studies showed that baicalein possesses a range of key pharmacological properties, such as reducing oxidative stress, anti-inflammatory properties, inhibiting aggregation of disease-specific amyloid proteins, inhibiting excitotoxicity, stimulating neurogenesis and differentiation action, and anti-apoptosis effects. Based on these properties, baicalein shows therapeutic potential for Alzheimer's disease and Parkinson's disease. In this review, we summarize the pharmacological protective actions of baicalein that make it suitable for the treatment of Alzheimer's disease and Parkinson's disease, and discuss the potential mechanisms underlying the effects.

Tongxie Formula Reduces Symptoms of Irritable Bowel Syndrome.

https://www.ncbi.nlm.nih.gov/pubmed/28634136
Clin Gastroenterol Hepatol. 2017 Jun 17. pii: S1542-3565(17)30733-4. doi:10.1016/j.cgh.2017.06.026.
By Fan H, Zheng L, Lai Y, Lu W, et al., China Irritable Bowel Syndrome Consortium

Abstract

BACKGROUND & AIMS:

Irritable bowel syndrome (IBS) is the most common chronic gastrointestinal disorder, yet few drugs are effective in reducing symptoms. Approximately 50% of patients with IBS attempt herbal therapy at least once. We performed a randomized controlled trial to compare the efficacy of the herb formulation tongxie vs placebo or pinaverium (an antispasmodic agent) in reducing symptoms of IBS.

METHODS:

We performed a trial of 1044 adult patients with IBS (based on Rome III criteria) at 5 hospitals in China, from August 2012 through January 2015. Subjects were randomly assigned (1:1:1) to groups given tongxie (a combination of A macrocephalae, P lactiflora, C reticulata, S divaricata, C pilosula, C wenyujin, C medica, and P cocos, along with other herbs, based on patient features), placebo, or pinaverium (50 mg tablets) 3 times daily for 4 weeks. Tongxie was personalized and prepared to avoid type II error. A questionnaire was used to assess the credibility of the placebo and calculate the Cronbach coefficient. Primary end points were significantly greater reductions in abdominal pain and Bristol stool score (before vs after the 4-week study period) in patients given tongxie compared with patients given placebo or pinaverium. Secondary end points were reductions in pain and stool frequencies and abdominal discomfort and its frequency. Categorical data were compared using the $\chi 2$ test or Fisher's exact test; continuous data were compared using the student t test.

RESULTS:

Subjects given tongxie had significant reductions, before vs after the study period, in all 6 symptoms assessed, compared to patients given placebo ($P<.001$). A significantly higher proportion of patients given tongxie had increased stool consistency (75.6%) than patients given pinaverium (50.6%), and a significantly higher proportion of patients given tongxie had fewer daily stools (72.7%) than subjects given pinaverium (58.3%) ($P<.001$ for both). However, significantly higher proportions of patients given pinaverium had reduced pain (63.5%) and pain frequency (69.5%) than patients given tongxie (51.4% and 58.6%, respectively; $P<.005$ for both).

CONCLUSION:

In a randomized controlled trial of patients with IBS in China, we found 4 weeks of tongxie to produce

significantly greater reduction in symptoms than placebo, and greater increases in stool consistency and reductions in stool frequency, than patients given pinaverium. Tongxie can therefore be considered an effective alternative therapy for patients with IBS who do not respond well to conventional therapies. The ingredients in tongxie appear to reduce symptoms through mechanisms similar to those of conventional IBS therapies. Clinical trials.gov no: NCT01641224.

Targeting Tumour microenvironment: Effects of Chinese Herbal Formula on Macrophage-Mediated Lung Cancer in Mice.

https://www.ncbi.nlm.nih.gov/pubmed/28630636
Evid Based Complement Alternat Med. 2017;2017:7187168. doi: 10.1155/2017/7187168.
By Xu F, Cui W, Zhao Z, Gong W, Wei Y, Liu J, Li M, et al.,

Abstract

Our previous studies have shown that Qing-Re-Huo-Xue (QRHX) formulae had significant anti-inflammatory effects in chronic airway diseases such as asthma and chronic obstructive lung disease. Here, we examined the effects of QRHX on lung cancer cell invasion and the potential associated mechanism(s), mainly polarization of macrophages in the tumor microenvironment. In vivo, QRHX both inhibited tumor growth and decreased the number of tumor-associated macrophages (TAMs) in mice with lung cancer. Further study indicated that QRHX inhibited cancer-related inflammation in tumor by decreasing infiltration of TAMs and IL-6 and TNF-*α* production and meanwhile decreased arginase 1 (Arg-1) expression and increased inducible NO synthase (iNOS) expression. QRHX could markedly inhibit CD31 and VEGF protein expression. Additionally, CXCL12/CXCR4 expression and JAK2/STAT3 phosphorylation were reduced in QRHX treatment group. Thus, we draw that QRHX played a more important role in inhibiting tumor growth by regulating TAMs in mice, which was found to be associated with the inhibition of inflammation and the CXCL12/CXCR4/JAK2/STAT3 signaling pathway.

Antrodia cinnamomea reduces obesity and modulates the gut microbiota in high-fat diet-fed mice.

https://www.ncbi.nlm.nih.gov/pubmed/28630461
Int J Obes (Lond). 2017 Jun 20. doi: 10.1038/ijo.2017.149. [Epub ahead of print]
By Chang CJ, Lu CC, Lin CS, Martel J, Ko YF, Ojcius DM, Wu TR, et al.,

Abstract

BACKGROUND:

Obesity is associated with gut microbiota dysbiosis, disrupted intestinal barrier and chronic inflammation. Given the high and increasing prevalence of obesity worldwide, anti-obesity treatments that are safe, effective and widely available would be beneficial. We examined whether the medicinal mushroom Antrodia cinnamomea may reduce obesity in mice fed with a high-fat diet (HFD).

METHODS:

Male C57BL/6J mice were fed a HFD for eight weeks to induce obesity and chronic inflammation. The mice were treated with a water extract of A. cinnamomea (WEAC), and body weight, fat accumulation, inflammatory markers, insulin sensitivity and the gut microbiota were monitored.

RESULTS:

After eight weeks, the mean body weight of HFD-fed mice was 39.8±1.2 g compared with 35.8±1.3 g for the HFD+1% WEAC group, corresponding to a reduction of 4 g or 10% of body weight (P<0.0001). WEAC supplementation reduced fat accumulation and serum triglycerides in a statistically significant manner in HFD-fed mice. WEAC also reversed the effects of HFD on pro-inflammatory markers (IL-1β, IL-6, TNF-α), insulin resistance and adipokine production (leptin and adiponectin). Notably, WEAC increased the expression of intestinal tight junctions (zonula occludens-1 and occludin) and antimicrobial proteins (Reg3g and lysozyme C) in the small intestine, leading to reduced blood endotoxemia. Finally, WEAC modulated the composition of the gut microbiota, reducing the Firmicutes/Bacteroidetes ratio and increasing the level of Akkermansia muciniphila and other bacterial species associated with anti-inflammatory properties.

CONCLUSIONS:

Supplementation with A. cinnamomea produces anti-obesogenic, anti-inflammatory, and antidiabetic effects in HFD-fed mice by maintaining intestinal integrity and modulating the gut microbiota.

Involvement of the glutamate/glutamine cycle and glutamate transporter GLT-1 in antidepressant-like effects of Xiao Yao san on chronically stressed mice.

https://www.ncbi.nlm.nih.gov/pubmed/28629384
BMC Complement Altern Med. 2017 Jun 19;17(1):326. doi: 10.1186/s12906-017-1830-0.
By Ding XF, Li YH, Chen JX, Sun LJ, Jiao HY, Wang XX, Zhou Y

Abstract

BACKGROUND:

Xiao Yao San (XYS) is an herbal prescription which is used in the treatment of depression for thousands of years from Song dynasty in China (960-1127 A.D.), and is the bestselling and most popular herb formula for treating major depression. This study aimed to assess the chronic antidepressant effects of XYS and fluoxetine in depressed mice induced by chronic unpredictable mild stress (CUMS) and its association with alterations in glutamate/glutamine cycle and glutamate transporters.

METHODS:

Mice in the control and model group were given 0.5 ml physiological saline by intragastric administration. Mice in two treatment groups were given XYS (0.25 g/kg/d) and fluoxetine (2.6 mg/kg/d), respectively. The depressive-like behaviors such as forced swim test (FST), sucrose preference test (SPT) and novelty-suppressed feeding (NSF) test were measured after mice exposed to CUMS for 21 days. Body weight, contents of glutamate and glutamine, glutamine/glutamate ratio that is usually thought to reflect glutamate/glutamine cycle, and the protein and mRNA expressions of glutamate transporters (excitatory amino acid transporter 1-2,GLAST/EAAT1 and GLT-1/EAAT2) were measured. The immunoreactivities of GLAST and GLT-1 in the hippocampus were also investigated.

RESULTS:

After CUMS exposure, mice exhibited depressive-like behaviors, body weight loss, increased glutamate level, decreased glutamine level, elevated glutamine/glutamate ratio, decreased GLT-1 protein expression and mRNA level, and decreased average optical density (AOD) of GLT-1 in the CA1, CA3 and DG in the hippocampus. These abnormalities could be effectively reversed by XYS or fluoxetine treatment. In addition, the

study also found that GLAST expression in the hippocampus could not be altered by 21-d CUMS.

CONCLUSION:

The studies indicated that XYS may have therapeutic actions on depression -like behavior s induced by CUMS in mice possibly mediated by modulation of glutamate/glutamine cycle and glutamate transporter GLT-1 in the hippocampus.

XuefuZhuyu decoction protected cardiomyocytes against hypoxia/reoxygenation injury by inhibiting autophagy.

https://www.ncbi.nlm.nih.gov/pubmed/28629357
BMC Complement Altern Med. 2017 Jun 19;17(1):325. doi: 10.1186/s12906-017-1822-0.
By Shi X, Zhu H, Zhang Y, Zhou M, Tang D, Zhang H

Abstract

BACKGROUND:

XuefuZhuyu decoction (XFZY) is a well-known traditional Chinese herbal medicine for the treatment of various cardiovascular diseases, such as unstable angina pectoris and myocardial ischemia-reperfusion injury. However, the mechanism by which XFZY contributes to the amelioration of cardiac injury remains unclear.

METHODS:

H9C2 cells were cultured under the hypoxic condition for 10 h and reoxygenated for 2 h. In the presence of various concentrations of XFZY for 12 h, the cell viability was measured by MTT assay. The protective effect of XFZY in hypoxia/reoxygenation (H/R) cell model was confirmed by measuring the amount of LDH released into the extracellular fluid. Cell apoptosis was measured by western blotting. The autophagy level of H9C2 cells and the correlative pathway were determined by transmission electron microscopy, Cyto-ID® Autophagy Detection Kit, and western blotting.

RESULTS:

In this study, we investigated the effects of XFZY on H/R induced cardiac injury. The results showed that treatment with XFZY significantly inhibited autophagy induced by H/R, with decreased formation of autophagosomes as well as the expression of LC3-II/LC3-I ratio and Beclin 1 after H/R. Importantly, inhibition of autophagy by XFZY resulted in enhanced cell viability and

decreased apoptosis. XFZY also inhibited the activation of AMPK and upregulated the phosphorylation of mammalian target of Rapamycin (mTOR).

CONCLUSIONS:

The cardioprotective effects of XFZY during H/R were mediated by inhibiting autophagy via regulating AMPK-mTOR signaling pathways.

Polysaccharides from Epimedium koreanum Nakai with immunomodulatory activity and inhibitory effect on tumor growth in LLC-bearing mice.

https://www.ncbi.nlm.nih.gov/pubmed/28627460
J Ethnopharmacol. 2017 Jun 13. pii: S0378-8741(17)30590-1. doi: 10.1016/j.jep.2017.06.014.
By Wang C, Feng L, Su J, Cui L, Dan Liu, Yan J, Ding C, Tan X, Jia X

Abstract

ETHNOPHARMACOLOGICAL RELEVANCE:

Epimedium koreanum Nakai is documented as tonic herbal in China for over a thousand years and has the potential to enhance the body's immunity according to the theory of traditional Chinese medicine. Polysaccharides are one of the most important effective compounds in Epimedium koreanum Nakai. Accumulating evidence indicated polysaccharides derived from traditional Chinese medicine have potent immune-enhancing properties and relatively nontoxic effects in cancer treatment. However, information about immunological regulation in tumor of Epimedium koreanum Nakai polysaccharides is limited and the reports of purification, characterization of polysaccharides have remained less. The purpose of our study was to further investigate the active polysaccharides from Epimedium koreanum Nakai by evaluating the immune-regulation activities in tumor-bearing mice and provide reasonable explanation for traditional application.

MATERIALS AND METHODS:

We firstly purified Epimedium koreanum polysaccharide (EPS) from crude extracts and evaluated EPS in vitro using immunological experiments including maturation and Ag presentation function of DCs, CD4 T-cell differentiation and secretion of anti-cancer cytokines. In LLC-bearing mice model, we investigated its

antitumor activities through evaluation of tumor cell proliferative activity, calculation of immune organ indexes and relative host immune system function tests.

RESULTS:

Results showed that EPS (180×10^4Da) was composed of mannose (Man), rhamnose (Rha), glucuronic acid (GlcUA), galactosamine (GalN), glucose (Glc), galactose (Gal), arabinose (Ara) and fructose (Fuc). Chemical composition assay indicated EPS was a fraction with 28.20% uronic acid content. FT-IR suggested the presence of pyraoid ring in EPS and SEM displayed smooth surface embedded by several pores. Moreover, Our study suggested EPS could remarkably stimulate macrophages to secrete substantial anti-cancer cytokines and promote maturation as well as Ag presentation function of DCs. Strikingly, CD4 T-cell differentiation and increased INF-γ production stimulated by EPS-activated macrophages were observed in the research. Furthermore, EPS exhibited prominent antitumor activities through regulating host immune system function in LLC-bearing mice. Taken together, experimental findings suggested EPS could be regarded as a potential immune-stimulating modifier for cancer therapy.

CONCLUSION:

Our studies demonstrated the polysaccharide (180×10^4Da) purified from Epimedium koreanum Nakai could promote maturation and Ag presentation function of DCs, increase the level of immunomodulatory cytokines and activate CD4 T-cell differentiation. Furthermore, it may inhibit the tumor growth in LLC-bearing mice through regulating host immune system function.

Chinese herbal medicine Xinji pill protects the heart from ischemia/reperfusion injury through the Akt/Nrf2 pathway.

https://www.ncbi.nlm.nih.gov/pubmed/28627591
Mol Med Rep. 2017 Jun 8. doi: 10.3892/mmr.2017.6732. [Epub ahead of print]
By Yuan Q, Chen R, Zheng X, Meng M, Kao Y, Liu J, Gan X, Shi M, Fu J, et al.,

Abstract

The cardioprotective drugs used for treatment against ischemia/reperfusion (MI/R) injury have been well evaluated and are considered inadequate. The Chinese herbal medicine formula, Xinji pill (XJP) has been used

traditionally for the prevention and treatment of ischemic heart diseases for decades. In the present study, the cardioprotective effects of XJP against MI/R injury were assessed in vivo and its possible mechanism was examined. Male Sprague-Dawley rats were selected for establishing an MI/R model, which was induced by ischemia for 30 min followed by 24 h reperfusion. Drugs and saline were administered intragastrically from day 14 prior to MI/R. Blood samples were collected for biochemical detection. The rats were then sacrificed and cardiac muscle tissues were harvested. The mRNA expression levels of antioxidant genes were measured by reverse transcription-quantitative polymerase chain reaction and the protein levels were measured by western blotting. Pretreatment with XJP for 14 days protected the heart against I/R-induced against heart injury, as demonstrated by normalized serum levels of lactate dehydrogenase and creatine kinase, and suppressed oxidative stress. XJP markedly upregulated the expression of antioxidant genes, including superoxide dismutase, catalase, glutathione reductase and glutathione peroxidase, and promoted the protein expression of heme oxygenase-1 and NFE2-related factor 2 (Nrf2) in the heart tissues. Furthermore, Akt kinase was confirmed to be upstream of Nrf2 in the XJP treatment. LY294002, a specific inhibitor of Akt, significantly eliminated the cardioprotective effects of XJP. In conclusion, these results demonstrated that XJP exhibited notable cardioprotective properties, in which the Akt/Nrf2 signaling pathway may be involved.