Journal of Traditional and Complementary Medicine Vol. 1, No. 1, pp. 8-24

Journal of Traditional and Complementary Medicine
Journal homepage http://www.jtcm.org

Anti-inflammatory activity of traditional Chinese medicinal herbs

Min-Hsiung Pan[1,*], Yi-Shiou Chiou[1], Mei-Ling Tsai[1], and Chi-Tang Ho[2,*]

[1] Department of Seafood Science, National Kaohsiung Marine University, Kaohsiung 811, Taiwan.
[2] Department of Food Science, Rutgers University, New Brunswick, New Jersey 08901-8520, USA.

Abstract

Accumulating epidemiological and clinical evidence shows that inflammation is an important risk factor for various human diseases. Thus, suppressing chronic inflammation has the potential to delay, prevent, and control various chronic diseases, including cerebrovascular, cardiovascular, joint, skin, pulmonary, blood, lymph, liver, pancreatic, and intestinal diseases. Various natural products from traditional Chinese medicine (TCM) have been shown to safely suppress proinflammatory pathways and control inflammation-associated disease. *In vivo* and/or *in vitro* studies have demonstrated that anti-inflammatory effects of TCM occur by inhibition of the expression of master transcription factors (for example, nuclear factor-κB (NF-κB)), pro-inflammatory cytokines (for example, tumor necrosis factor-α (TNF-α), chemokines (for example, chemokine (C-C motif) ligand (CCL)-24), intercellular adhesion molecule expression and pro-inflammatory mediators (for example, inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX2)). However, a handful of review articles have focused on the anti-inflammatory activities of TCM and explore their possible mechanisms of action. In this review, we summarize recent research attempting to identify the anti-inflammatory constituents of TCM and their molecular targets that may create new opportunities for innovation in modern pharmacology.

Key words: Anti-inflammatory activity, Traditional Chinese medicinal herbs, Pro-inflammatory cytokines

Inflammation and chronic disease

Inflammation is known to contribute to physiological and pathological processes by the activation of the immune system, local vascular system, and various cells within the damaged tissue (Coussens and Werb, 2002). Prolonged inflammation, known as chronic inflammation, is caused by a variety of factors, including microbial pathogen infection, physical, chemical, and surgical irritation, and/or wounding. The classical characteristics of inflammation are pain, swelling, edema, redness and heat (Mantovani, 2010). There is now growing evidence supporting the concept that chronic inflammation may affect many organ systems including skin, brain, colon, blood vessels, pancreas, joints, lung, and heart (Khatami, 2009).

Epidemiological studies have also revealed that chronic inflammation is causally linked to various human diseases, including cerebrovascular, cardiovascular, joint, cutaneous, pulmonary, blood, liver, and intestinal diseases as well as diabetes (Figure1). The inflammatory process leads to the up-regulation of a series of pro-inflammatory enzymes, cytokines, reactive oxygen/nitrogen species (RO/NS) and signaling

Correspondence to:
Dr. Min-Hsiung Pan, Department of Seafood Science, National Kaohsiung Marine University, No.142, Haijhuan Rd., Nanzih District, Kaohsiung 81143, Taiwan, Tel: +886-7-361-7141 ext 3623, Fax: +886-7-361-1261, E-mail: mhpan@mail.nkmu.edu.tw
Dr. Chi-Tang Ho, Department of Food Science, Rutgers University, 65 Dudley Road, New Brunswick, NJ 08901, USA, Tel: +1-732-932-9611 ext 235, Fax: +1-732-932-6776, E-mail: ho@aesop.rutgers.edu

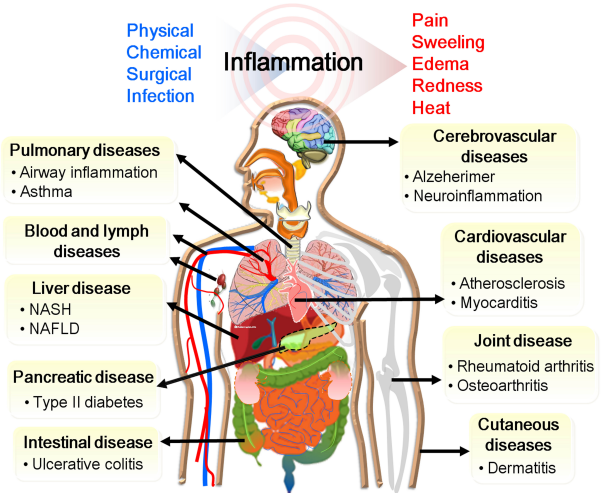


Figure 1. Human diseases linked with chronic inflammation

proteins in infected tissues and cells. Elevation in both the tissue and the serum levels of pro-inflammatory mediators predict an increased health risk at all stages of these diseases (Forrester and Bick-Forrester, 2005). Thus, blocking of inflammatory signaling is usually recognized as a potential therapeutic modality for chemoprevention.

TCM herbs as promising anti-inflammatory agents

TCM has evolved over the past 5,000 years to prevent and manage human disease. The clinical recognition and diagnosis of disease in TCM are mainly based on the yin-yang and five elements theories (Lu et al., 2009a). Traditionally, the two most common methods of applying herb treatments are to make a decoction (a strong tea that must be simmered for an hour or more) and to make large pills containing honey as a binding agent. However, modern herbs, developed to replace the standard Chinese preparations, come in two popular forms, namely, extract powders (or granules) and smooth (Wang et al., 2009). Herbs used in TCM and their active components have been demonstrated in many animal or cell culture models to inhibit inflammatory responses in different organs including the lung, esophagus, cerebrum, colon, skin, prostate, mammary glands, liver, pancreas, and lung (Pan et al., 2011; Ichikawa et al., 2003; Yarosh et al., 2006). Table 1 summarizes the various natural products derived from TCM herbs, which have been shown to safely suppress proinflammatory signaling pathways and to control inflammation- associated disease.

Anti-inflammatory properties in chronic diseases and its possible mechanisms

Blood and lymph diseases

The human's immune system is composed of organs such as the spleen and thymus along with lymph nodes and bone marrow that also contribute to the prevention of infection and disease by producing and storing specific immune cells (Schmid-Hempel, 2005). Indeed, inflammation is an integral part of the immune system, but sometimes chronic inflammation becomes a pathophysiological process leading to disease development and progression (Handschin and Spiegelman, 2008).

Macrophages play a central role in chronic inflammation by mechanisms such as the overproduction of pro-inflammatory cytokines (tumor necrosis factor-α (TNF-α and interleukins (IL-6 and IL-1β) and generation of inflammatory mediators in response to microbial products (LPS, lipopolysaccharide), such as reactive oxygen species (ROS), prostaglandin E_2 (PGE_2), nitric oxide (NO) and interferon-γ (IFN-γ). These mediators are potent activators of components of the pro-inflammatory signal transduction cascade, including NF-κB-inducing kinase, mitogen-activated protein kinase (MAPK), and protein kinase C (PKC) (Pan et al., 2009a). 6-gingerol, 6-shogaol, andrograpanin, phylligenin, tectorigenin, rhein, baicalin, berberine, naringenin, cimiracemate A, ligustilide and schicantherin A are bioactive substances in medicinal plants that have been reported to decrease LPS and/or IFN-γ-induced production of pro-inflammatory cytokines and mediators in macrophages and primary mouse splenocytes by down-regulation of MAPK and inhibition of PKC- mediated activation of downstream transcription factors NF-κB and activator protein 1 (AP-1) (Lee et al., 2009c; Lim et al., 2008; Dugasani et al., 2010; Liu et al., 2008a; Ling et al., 2010; Zhang et al., 2010a; Pan et al., 2008; Luo et al., 2009; Li et al., 2011b; Lin et al., 2008; Ho and Lin, 2008; Lin and Lin, 2011; Hwang et al., 2011; Yang et al., 2009; Su et al., 2011). Recently, evodiamine extracted from Evodiae Fructus (吳茱萸 wú zhū yú; the fruits of *Evodia rutaecarpa*), was also demonstrated to be effective in inhibiting the production of COX-2-mediated PGE_2 and expression of iNOS through inhibition of PI3K/Akt/p70S6K signaling and inhibition of hypoxia-inducible factor-1α (HIF-1α) accumulation in hypoxia-stimulated RAW 264.7 macrophages (Liu et al., 2009b).

Cerebrovascular diseases

Recent studies have shown that the severity of cerebrovascular disease, including Alzheimer's disease, Parkinson's disease and cerebral ischemia, correlates with inflammation-mediated responses in neural cells (Britschgi and Wyss-Coray, 2007). Inflammation of the brain and central nervous system (CNS) are also mediated by the generation of various pro-inflammatory cytokines, including TNF-α, IL-1β and IL-6 in microglia, astrocytes, ependymal cells, macrophages and mast cells (Rivest, 2009). Moreover, microglia activation is one of the causative factors in neuroinflammation, which results in brain damage during neurodegenerative disease. Previous studies have shown that luteolin, senkyunolide A, Z-ligustilide and Agrimoniae Herba possess anti-inflammatory properties by decreasing LPS-induced NO and PGE_2 production, by suppressing TNF-α, IL-1β, iNOS and COX-2 expression, and by blocking NF-κB activation in murine BV-2 microglial cells (Zhu et al., 2011b;Or et al., 2011b;Bae et al., 2010). *In vivo* studies have shown that cholalic acid, hyodeoxycholalic acid and total glucosides of peony (TGP) can prevent cerebral ischemia and Alzheimer's disease by inhibiting inflammatory cytokine (TNF-α, IL-1β and IL-6) production and down-regulating c-Jun N-terminal kinases (JNK), p-38 and MAPK extracellular signal-regulated kinases (ERK) kinase3/6 (MEK3/6) phosphorylation (Huang et al., 2011; Hua et al., 2009).

Cardiovascular diseases

Recent studies have demonstrated that inflammatory responses may cause myocardial damage and atherosclerosis, leading causes of cardiovascular disease (CVD) (Libby, 2006).

Tanshinone IIA and curcumin, substances with strong anti-inflammatory activity, have been shown to be effective in protecting against cardiac inflammation in *in vitro* and *in vivo* models (Ren et al., 2010; Pari et al., 2008). Mito et al. (Mito, 2011) reported that the cardioprotective effects of curcumin are elicited through the inhibition of IL-1I, TNF-α, GATA-4 and NF-κB expression and may provide a novel therapeutic strategy for the treatment of autoimmune myocarditis. In addition, Salviae Miltiorrhizae Radix (丹參 dān shēn; the roots of *Salvia miltiorrhiza* Bunge) preparations rich in tanshinone IIA were shown to reduce infarct size and improve cardiac apoptosis and inflammation by significantly enhancing Akt phosphorylation and suppressing NF-κB phosphorylation, myeloperoxidase (MPO) activity and production of inflammatory cytokines, such as TNF-α, and IL-6 (Zhang et al., 2010b). Clinical studies have shown that vascular inflammation is the earliest event in the development of atherosclerosis (Izumimoto and Kawakami, 2011). The process involves stimulation of cholesterol and oxidized low density lipoprotein (ox-LDL) accumulation within the vessel wall and generation of oxidative free radicals, which activate vascular endothelial cells and enhance the adhesion of monocytes to them by promoting expression of endothelial adhesion molecules, including selectins, vascular cell adhesion molecule-1 (VCAM-1) and intracellular adhesion molecule-1 (ICAM-1) (Libby and Theroux, 2005). Once monocytes firmly attach to the surface of the endothelium under the influence of chemoattractants such as monocyte chemoattractant protein-1 (MCP-1), they transmigrate into the arterial intima and differentiate into macrophages. These macrophages proliferate and amplify the inflammatory response through the secretion of numerous growth factors, adhesion molecules, pro-inflammatory cytokines (IL-6, IL-1β and TNF-α) and matrix metalloproteinases (MMPs) (Packard and Libby, 2008). In addition, the toll-like receptors (TLRs) TLR-2 and TLR-4 also play an important role in innate immune and inflammatory responses, and several reports have demonstrated the expression of TLR-2 and TLR-4 in atherosclerotic lesions (Schoneveld et al., 2008). TGP, ginsenoside, ginkgolide B, monacolin K and glycyrrhetinic acid have been shown in experimental animal studies and *in vitro* studies of human umbilical vein endothelial cells (HUVEC) to significantly attenuate the development of atherosclerotic disease by decreasing ROS generation, reducing expression of adhesion molecules, MMP-2 and pro-inflammatory mediators and increasing macrophage migration inhibitory factor (MIF) levels (Li et al., 2009; Chang et al., 2010; Xie et al., 2011; Li et al., 2008; Li et al., 2011a; Liu et al., 2008b; Liu et al., 2010b).

Pancreatic disease

Mounting evidence suggests that oxidative stress and chronic inflammation play an important role in obesity-related metabolic disorders such as type 2 diabetes (Hotamisligil, 2006). However, type 1 diabetes, one of the most common autoimmune diseases, is caused by T cell- mediated destruction of pancreatic beta cells (Kalousova et al., 2004). More and more evidence indicates that the anti-inflammatory effects of TCM may contribute to their antidiabetic action (Xie and Du, 2011).

Recent studies have shown that berberine can ameliorate type 1 diabetes and decrease the expression of Th17 cytokines in nonobese diabetic (NOD) mice via suppression of Th17 and Th1 differentiation. Berberine inhibited Th1 differentiation by decreasing the activity of STAT1 and STAT4 through suppression of p38 MAPK/JNK activity, but down-regulated Th17 differentiation through activation of ERK1/2 and reduction in the levels of STAT3 phosphorylation and retinoic acid-related orphan receptor γt (RORγt) expression (Cui et al., 2009).

Recently, the active principles in Astragali Radix (黄耆 huáng qí) (calycosin, calycosin-7-β-D-glucoside, ononin, calycosin and formononetin) that inhibit pro-inflammatory cytokine production were identified. Xu et al. (Xu et al., 2011) have reported that calycosin can inhibit advanced glycation end products (AGEs)-induced macrophage migration and adhesion to endothelial cells; calycosin also can relieve local inflammation by reducing expression of transforming growth factor-β1(TGF-β1), ICAM-1, p-ERK 1/2, p-NF-κB and receptor for advanced glycation end products (RAGE) and by increasing expression of the estrogen receptor in HUVECs (Xu et al., 2011). In another study, it was demonstrated that four natural compounds from Astragali Radix (黄耆 huáng qí) with anti-diabetic and insulin sensitizing effects can reduce the secretion of pro-inflammatory cytokines (TNF-α, IL-6 and MCP-1) and expression levels of inflammatory cell markers (CD68 and F4/80) and increase the level of agrinase I (Hoo et al., 2010).

This major increase in morbidity and mortality of diabetes is due to the development of both macro- and micro-vascular complications such as are commonly found in diabetic patients with foot ulcers (Levin, 2002). Previous scientific studies reported that Rehmanniae Radix (地黄 dì huáng) was effective in promoting diabetic foot ulcer healing, angiogenesis, and tissue regeneration and in inhibiting inflammation through induction of vascular endothelial growth factor (VEGF) expression, reduction of LPS-induced NO production, stimulation of human fibroblast cell (Hs27) proliferation and promotion of HUVEC cell migration and tube formation (Lau et al., 2009; Tam et al., 2011).

Intestinal disease

The major forms of inflammatory bowel disease (IBD), i.e., Crohn's disease and ulcerative colitis (UC), are chronic relapsing inflammatory conditions of the gastrointestinal tract, resulting from impairment of intestinal epithelial barrier function and subsequent defects in adaptive immunity (Tsianos and Katsanos, 2009). Increasing evidence demonstrates that infiltration and migration of innate immune cells depends on production of pro-inflammatory cytokines, chemokines and adhesion molecules (Jose et al., 2006). In addition, the inflammatory reaction involves complex interactions between immune cells and endothelial cells (ECs), the monolayer between blood and tissue (Bouguen et al., 2011). Therefore, restoration of the balance between pro- and anti-inflammatory cytokines may be a promising strategy for the treatment of IBD. Recent studies have shown that mollugin inhibits TNF-Ŭ -induced inflammatory responses and chemotaxis in HT-29 cells and U937 cells through inhibition of NF-əB activation and decreased MCP-1, IL-8 and ICAM-1 expression (Kim et al., 2009). In another model it has also been found that matrine, berberine, hypaconitine and skimmianine could inhibit the LPS-stimulated inflammatory reaction by improving NO-dependent vasomotion and inhibiting expression of inflammatory mediator (IL-6, IL-8, soluble ICAM-1, TNF-α LBP, and PGE_2) (Zhang et al., 2011;Suo et al., 2009). The colitis model in rats has indicated that berberine, hypaconitine, skimmianine, oxymatrine and rhubarbs can ameliorate acetic acid- and 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis and bowel pain via decreases in TNFα, LBP, IL-12, TLR-4 and NF-κB activation and increases in the IL-10 level, resulting in an improved balance of Th1 and Th2 cells (Zhang et al., 2011; Fan et al., 2008; Liu et al., 2009a).

Pulmonary diseases

Respiratory epithelium plays a key role in airway inflammatory disease, including asthma, acute and chronic microbial infections, and obstructive pulmonary disease by the production of numerous cytokines, chemokines, inflammatory enzymes, and adhesion molecules (Iwamoto, 2003). Importantly, balance of Th1-Th2 cytokine secretion has been suggested as necessary to maintain healthy immune homeostasis. Imbalance has been hypothesized to underlie allergic asthma through a shift in immune responses from a Th1 (IFN-γ) pattern toward a Th2 (IL-4, IL-5, and IL-13) profile, which promotes IgE production, eosinophilic inflammation, activation and survival, and enhanced airway smooth muscle contractility (Busse and Rosenwasser, 2003). Previous studies also suggest that lung epithelial cells are involved in inflammatory processes by recruiting immune cells and producing pro-

inflammatory cytokines, resulting in amplification of the inflammatory signal (Lee et al., 2007). Recent studies showed that ursolic acid, triptolide and Viticis Fructus (蔓荊子 màn jīng zǐ; the fruits of *Vitex rotundifolia*) extract could suppress Th2 cell proliferation, eosinophil migration and neutrophilic inflammation by down-regulation of cytokines, chemokines and cell adhesion molecules (Lee et al., 2007; Lee et al., 2008; Hoyle et al., 2010; Sohn et al., 2009). We found that Visci Ramus (槲寄生 hú jì shēng; the dried stem, with leaf *Viscum coloratum*), Ganoderma (靈芝 líng zhī; *Ganoderma lucidum*), Sophorae Flavescentis Radix (苦參 kǔ shēn) and Glycyrrhizae Radix (甘草 gān cǎo) extract potently inhibited airway hyperresponsiveness (AHR) and reduced eosinophil infiltration of the lungs in ovalbumin (OVA)-sensitized mice by reducing levels of IgE, CCLs (CCL11 and CCL24) and Th2-associated cytokines (IL-5, IL-4 and IL-13), and by increasing IFN-IIsecretion (Busse et al., 2010; Shen et al., 2011). Polyphenol rich extracts from officinal magnolia bark (厚朴 hòu pò) and baicalin were also shown to alleviate pneumonia by decreasing the level of NO, IL-6, TNF-α and ICAM-1 and reducing NF-κB and Toll like receptor (TLR)-3 expression in *Pneumocystis carinii* and influenza virus A (IVA)-infected lung tissue (Wu et al., 2011; Zhou and Zhou, 2009).

Joint diseases

Rheumatoid arthritis (RA) is a systemic and chronic inflammatory autoimmune disorder characterized by synovial hyperplasia, inflammatory cell infiltration and angiogenesis, which ultimately lead to cartilage erosion and articular destruction (Leff, 2006). Several inflammatory cytokines, such as TNF-α, IL-1β, IL-6, IL-33 and rheumatoid factor (RF) not only play important roles in the chronic inflammation of human RA, but are also associated with various manifestations of inflammation-related angiogenesis (Marrelli et al., 2011).

In the rat model of arthritis, the extract of Arisaematis Rhizoma (天南星 tiān nán xīng; the root of *Arisaema rhizomatum*), scopolin and kirenol inhibited paw and joint swelling by suppressing inflammatory cytokines and NO production, inhibiting VEGF and fibroblast growth factor (FGF-2) expression and up-regulating Annexin-1 which interacts with NF-κB to inhibit NF-κB activity (Chunxia et al., 2011; Wang et al., 2011; Pan et al., 2009b). Liu et al. (Liu et al., 2010a) also demonstrated that icariin can protect chondrocytes from LPS-induced inflammation and extracellular matrix degradation through inhibition of NO, MMP, iNOS and COX-2 expression. The direct anti-inflammatory and analgesic effects of TCM were observed in animal models of both acute and subacute inflammation, such as formalin-induced paw licking, carrageenan-induced paw edema, cotton pellet-induced granuloma, acetic acid-induced permeability, xylene-induced ear edema, collagen-induced arthritis, complete Freund's adjuvant (CFA)-induced joint inflammation and thermally induced pain.

Skin diseases

As the primary interface between the body and the external environment, the skin provides the first line of defense against traumatic injury and infection by microbial pathogens. Besides its properties as a physical barrier, the skin has many active defense mechanisms and regulation of these mechanisms is important because inappropriate or misdirected immune activity is implicated in the pathogenesis of a large variety of inflammatory skin diseases. High levels of pro-inflammatory cytokines and ROS are proposed to contribute to the pathophysiological mechanisms (Numerof et al., 2005). Lee *et al*. (Lee et al., 2009a; Lee et al., 2009b) found anti-inflammatory effects of the extract of wild chrysanthemum (野菊 yě jú; *Chrysanthemum indicum*, CIE) and Asparagi Radix (天門冬 tiān mén dōng; *Asparagus cochinchinensis* Merrill, ACE) in 12-O-tetradecanoyl-phorbol-13-acetate (TPA)-induced mouse ear edema and acetic acid-induced vascular permeability models. CIE and ACE showed potent inhibitory activity against topical edema of the mouse ear, leading to substantial reductions in skin thickness and tissue weight, inflammatory cytokine production (TNF-α and IL-1β, neutrophil-mediated MPO activity, and various histopathological indicators.

Liver disease

Most acute and chronic liver diseases are characterized by the presence of inflammatory and oxidative stress processes with enhanced expression of various pro-inflammatory cytokines and lipid mediators (Ferre and Claria, 2006; Tilg et al., 2006). In the non-alcoholic steatohepatitis (NASH) model, keishi-bukuryo-gan and Qu Yu Hua Tan Tong Luo decoctions have been found to relieve lipid peroxidation and inflammation of the liver by down-regulation of TNF-α, IL-8, cholesterol, triglycerides (TGs) and MDA levels and up-regulation of superoxide dismutase (SOD) activity (Fujimoto et al., 2010; Zhang et al., 2008).

Conclusion

Strong direct evidence suggests that chronic inflammation promotes development of numerous human diseases such as Alzheimer's, atherosclerosis, arthritis, asthma, diabetes and IBD. The Chinese herbs investigated are mostly qi supplementation (補氣 bǔ qì), heat-clearing (清熱 qīng rè) and toxin-resolving (解毒 jiě dú) drugs, as described previously in the theory of TCM (Xie and Du, 2011). TCM has a long history of human use, and the main active components recorded and identified, in heat-clearing and detoxifying Chinese herbs usually have widespread pharmacological effects including anti-inflammatory actions (Ren et al., 1994). Clinical trials have also demonstrated the effectiveness of TCM for the prevention and therapy of many chronic inflammatory diseases, and the related mechanisms have also been identified. Therefore, in this article, we systemically reviewed the evidence for the efficacy of anti-inflammatory products used in TCM in the treatment of inflammatory processes associated with various chronic diseases and shared their known mechanisms of action.

It is clear that natural bioactive compounds from herbs used in TCM can interfere with multiple cell signaling pathways and have multiple targets within the cells. These mechanisms include (a) modulation of inflammatory signal transduction pathways linked to NF-əB, AP-1, PI3K/Akt, MAPKs, STATs, and TLRs, (b) induction of antioxidant enzymes such as SOD, glutathione peroxidase (GPx) and glutathione reductase (GRx), (c) reduction of inflammatory molecule production including iNOS, COX-2, NO and PGE_2 (d) diminished recruitment and activation of inflammatory cells, (e) altered regulation of cellular functions and (f) changes in the balance of Th1 and Th2 cell-derived cytokines (Figure 1). Besides their influence on the regulation of intracellular signaling pathways, the active components from TCM may also inhibit expression of growth factors (VEGF, FGF-2 and TGF-β1) and MMPs, which are important cofactors for angiogenesis, wound repair and tissue regeneration.

This information adds to the body of evidence indicating that the products of TCM, because of their safety and anti-inflammatory efficacy, may have a potential role in the prevention and treatment of chronic inflammatory disease (Figure 2). Furthermore, extensive research is needed concerning the influence of active herbal products on the pathological, immunological, biochemical and molecular biology-related aspects of disease processes, which may ultimately lead to enhanced formulations for chemoprevention.

Acknowledgements

This study was supported by the National Science Council NSC 98-2313-B-022-002-MY3 and 099-2811-B-022-002

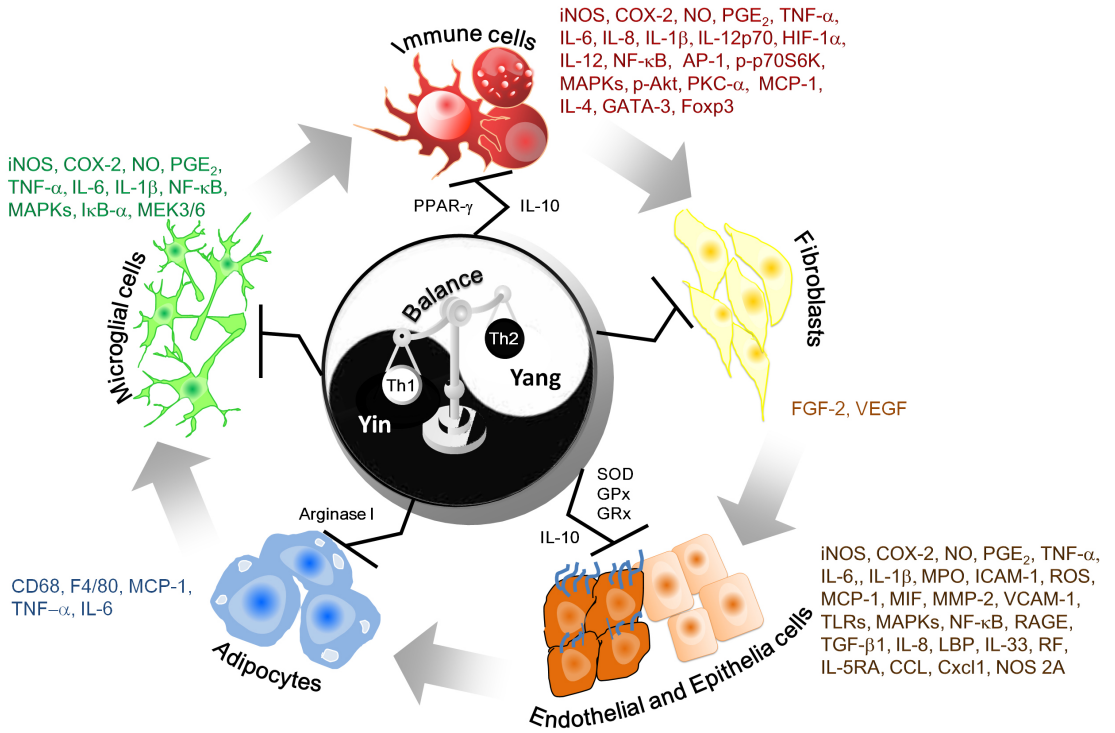
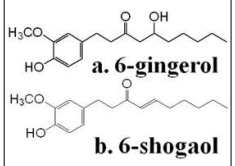
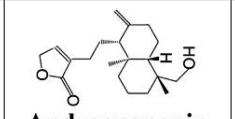
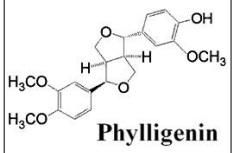
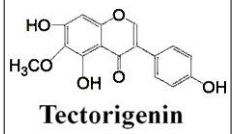
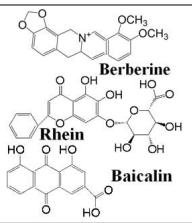
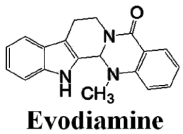
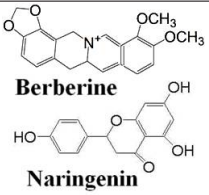
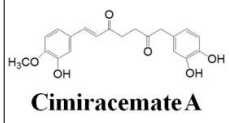
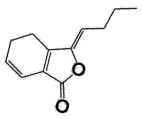
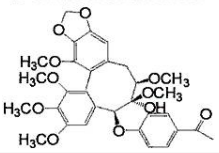
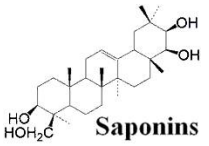
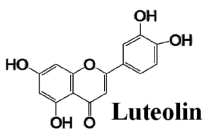
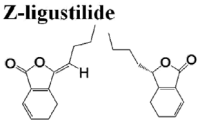
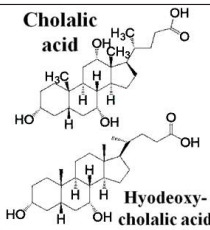
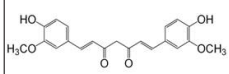
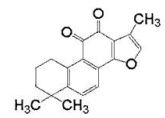
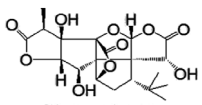
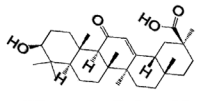
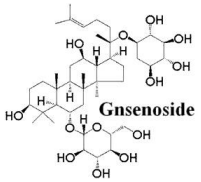


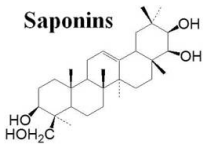
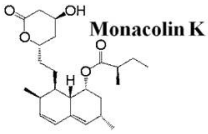
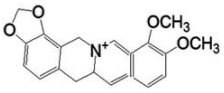
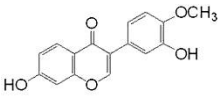
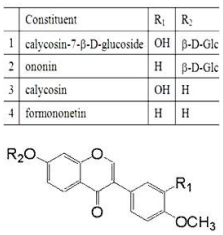
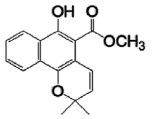
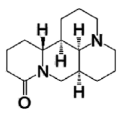
Figure 2. Effects of traditional Chinese medicine (TCM) mediated by the molecular mechanisms of anti-inflammatory action

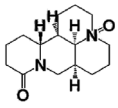
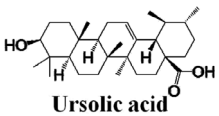
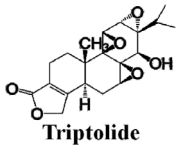
Table 1. Anti-inflammatory effects of the active components from TCM herbs

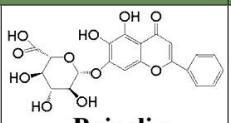
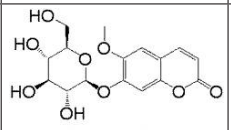
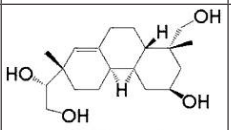
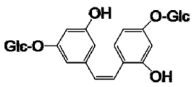
Group of diseases (target organ)	Chinese herbs		Experimental models Studied type (Dose)	Mechanism(s) of action (refs)
Blood and lymph diseases	Origin (pinyin)	Effective ingredient/ Decoction		
	 Zingiber officinale Roscoe (Sheng jiang)	 a. 6-gingerol b. 6-shogaol	a. LPS-stimulated macrophage cells (RAW264.7) (20-80 μM) b. LPS-induced RAW 264.7 cells (1-6 μM)	a. Decreases inducible nitric oxide synthase (iNOS) and tumor necrosis factor-α (TNF-α) expression by blocking nuclear factor-κB (NF-κB) and protein kinase C-α (PKC-α) signaling (Lee et al., 2009c) b. Reduces prostaglandin E_2 (PGE_2) and nitric oxide (NO) production (Dugasani et al., 2010)
	 Andrographis paniculata (Chuanxinlian)	 Andrograpanin	LPS-stimulated bone marrow-derived murine macrophage cells (1.5-90 μM)	Inhibits iNOS, TNF-Ŭ interleukin (IL)-6 and IL-12p70 expression and NO production by down-regulation of p38 mitogen-activated protein kinase (MAPKs) signaling pathways (Liu et al., 2008a)
	 Forsythia koreana (Nakai)	 Phylligenin	a. LPS-stimulated RAW264.7 cells (1-100 μM) b. λ-Carrageenan-induced paw edema in mice (12.5-100 mg/kg)	a. Inhibits cyclooxygenase-2 (COX-2)-mediated PGE_2 and iNOS-mediated NO synthesis by down-regulation of NF-κB signaling pathways b. Suppresses mouse carrageenan-induced paw edema (Lim et al., 2008)
	 Rasmulus mori (Sangzhi)	Mori Ramulus was extracted by EtoAc, n-BuOH and chloroform	LPS/Interferon-gamma (IFN-γ) stimulated macrophage cells	EtOAc and n-BuOH extractions: inhibits NO production (Ling et al., 2010)
	 Belamcanda chinensis (Shegan)	 Tectorigenin	LPS/ IFN-γ stimulated RAW264.7 cells (50-100 μM)	Decreases NO, IL-1β and PGE_2 production, and iNOS and COX-2 protein expression by blocking of NF-κB activation (Pan et al., 2008)
	 Anisomeles indica (Luo Ma Yi)	One cembrane-type diterpenoid Two benzenoids Five flavonoids Six phenyl propanoids	LPS/ IFN-γ stimulated peritoneal excluded macrophage cells (2-40 μM)	Decreases NO, TNF-Ŭand IL-12 production (Rao et al., 2009)
	 Ganoderma lucidum (Lingzhi)	Triterpenes and polysaccharides were extracted by 95% EtOH from *G. lucidum* (GLT)	a. LPS-induced RAW264.7 cells (3-50 (μg/mL) b. LPS-induced endotoxemic mice (12 mg/kg)	a. Reduces TNF-α, IL-6, PGE_2 and NO production, and protein expressions of iNOS and COX-2 by inhibiting ERK and JNK-mediated b. NF-κB and AP-1 activation. Inhibits the production of TNF-α and IL-6 (Dudhgaonkar et al., 2009)
	 Xiexin Decoction (Xie xin tang) Radix et Rhizoma Rhei Rhizoma Coptidis Radix Scutellaria	 Berberine Rhein Baicalin	a. LPS-stimulated RAW264.7 cells (0.3-10 μM) b. Intraperitoneal-injection of LPS (3.2 mg/kg) in male SD rats (oral administration, 3.34 g/kg)	Decreases NO production *in vitro* and *in vivo* (Xu, 2006)
	 Evodia rutaecarpa (Wu zhu yu)	 Evodiamine	Hypoxia (1% O_2)-induced RAW264.7 cells (0.3-3 μM)	Represses hypoxia-induced COX-2-mediated PGE_2 production and iNOS expression by down-regulation of p-Akt and p-p70S6K-mediated HIF-1α translational process (Liu et al., 2009b)
	 Berberis aristata (Yin du xiao bi) Citrus paradise (Putao you)	 Berberine Naringenin	LPS-stimulated primary mouse splenocytes (Berberine: 0.8-3.3 μM) (Naringenin: 18-70 μM)	Inhibits IL-6/IL-10 or TNF-α/IL-10 ratios (Lin and Lin, 2011)

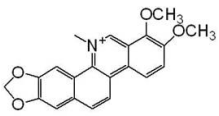
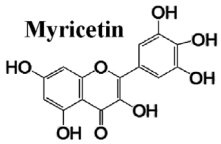
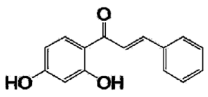
Group of diseases (target organ)	Chinese herbs		Experimental models Studied type (Dose)	Mechanism(s) of action (refs)
	 Houttuynia cordata thunb (Yuxingcao)	*Houttuynia cordata Thunb.* (HC) essential oil were extracted by steam distillation	LPS-induced mouse peritoneal macrophages (0.01-100 μg/mL)	Decreases PGE_2 production, COX-2 activity, and COX-2 gene and protein expression (Li et al., 2011b)
	 Cimicifuga rhizome (Sheng ma)	 Cimiracemate A	LPS-induced human primary blood macrophages (140 μM)	Inhibits TNF-α production by down-regulation of ERK and NF-κB activities (Yang et al., 2009)
	 Acanthopanax senticosus (Ci wu jia)	*Acanthopanax senticosus* extract (ASE)	LPS/ IFN-γ-stimulated RAW264.7 cells (100-1000 μg/mL)	Suppresses iNOS and NO production through the inhibition of intracellular peroxides levels and NF-κB activity (Lin et al., 2008)
	 Sargassum hemiphyllum	*S. hemiphyllum* sulfated polysaccharide extract (SHSP)	LPS-stimulated RAW264.7 cells (1-5 mg/mL)	Reduces TNF-T, IL-6, IL-1β and NO production, and RNA expressions of IL-1β, iNOS and COX-2 by down-regulation of NF-κB translocation (Hwang et al., 2011)
	 Citrus reticulatea (Chen pi)	Citrus fruit peels were extracted by heat treatment (naringin, hesperidin, nobiletin and tangeretin)	LPS-stimulated RAW264.7 cells (0.5-4 mg/mL)	Inhibits NO production, and iNOS gene expression (Ho and Lin, 2008)
	 Angelica sinensis (Danggui)	Ligustilide 	LPS-stimulated RAW264.7 cells (5-250 μM)	Suppresses NO, PGE_2 and TNF-α production by blocking the activation of p38MAPK, extracellular signal-regulated kinase (ERK1/2), c-Jun N-terminal kinase (JNK) and the downstream transcription factors AP-1 and NF-κB (Zhu et al., 2011b)
	 Schisandra sphenanthera (Wu wei zi)	Schisantherin A 	LPS-stimulated RAW264.7 cells (0.5-25 mg/mL)	Reduces TNF-α, IL-6, PGE_2 and NO production, and protein expressions of iNOS, and COX-2 by blocking NF-κB and MAPKs (JNK, p-38 and ERK) signaling (Ci et al., 2010)
	 Semen nigellae (Heizhongcaozi)	 Saponins	LPS/ IFN-γ -stimulated RAW264.7 cells	Suppresses NO production, iNOS, COX-2, IL-1β, IL-6 levels and increases peroxisome proliferator-activated receptor gamma (PPAR-γ) expression through ERK/ pathway (Zhang et al., 2010a)
	 Radix linderae (Wuyao)	Total alkaloids from Radix Linderae (TARL)	LPS-stimulated RAW264.7 cells (10-100 mg/mL)	Prevents NO, IL-1β and TNF-α production, and mRNA expressions of iNOS, IL-1β and TNF-α by blocking MAPKs (p-38 and ERK) and NF-κB p65 protein phosphorylation (Luo et al., 2009)
Cerebrovascular diseases (brain and neuron)				
Neuroinflammation	 Peanut shell (HuaSheng Ke)	 Luteolin	LPS-stimulated murine BV2 microglia (10-50 μM)	Suppresses NO and PGE_2 production, and TNF-TTTiNOS, COX-2 and IL-1β expression by blocking the activation of NF-κB signaling (Zhu et al., 2011a)
Alzheimer's disease	 Valeriana amurensis Smir. ex Kom. (Xie Cao)	Valeriana amurensis was extracted by 50% EtOH	Alzheimer's disease model rats' brain	Reduces iNOS, COX-2 and IκB-αB levels (Zhang et al., 2010c)

Group of diseases (target organ)	Chinese herbs		Experimental models Studied type (Dose)	Mechanism(s) of action (refs)
Alzheimer's disease	 Paeony (Mudan)	Total glucosides of paeony (TGP)	Fibrillar Abeta42 induced Alzheimer's disease (AD)	Decreases IL-1β, IL-6, p-p38, p-c-Jun N-terminal kinases (JNK) and MAP kinase kinase3/6 (MEK3/6) protein expressions (Huang et al., 2011)
Brain inflammation	 Agrimoniae herba (Xian he cao)		LPS-induced BV2 microglial cells (0.01-1mg/mL)	Suppresses TNF-Ű, IL-1β, IL-6 production and iNOS expression (Bae et al., 2010)
Neuroinflammation	 Ligusticum chuanxiong (Chuanxiong)	Z-ligustilide  Senkyunolide A	LPS-stimulated murine BV-2 microglial cells and human peripheral blood monocyte derived macrophages (25-50 μg/mL)	Increases the degradation of TNF-α and iNOS mRNA expressions and reduce TNF-α half life (Or et al., 2011a)
Focal Cerebral Ischemia	 Qing Kai Ling	Cholalic acid  Hyodeoxy-cholalic acid	Cerebral ischemia model in rat brain (21 mg/kg)	Decreases TNF-α and IL-1β levels (Hua et al., 2009)
Cardiovascular diseases (heart)				
Autoimmune myocarditis	 Curcuma longa (Jianghuang)	 Curcumin	Cardiac myosin-induced experimental autoimmune myocarditis (EAM) (50 mg/kg/d)	Against cardiac inflammation through suppression of IL-1β, TNF-α, GATA-4 and NF-κB expresses (Mito, 2011)
Cardiac inflammation	 Salvia miltiorrhiza Bunge (Danshen)	 Tanshinone IIA (TSN)	1. Myocardial ischaemia /reperfusion (I/R) injury in diabetic rats (5 mg/kg)	Decreases cardiac inflammation by enhancing PI3K/Akt pathway, suppressing NF-κB p65 protein phosphorylation and reducing of myeloperoxidase (MPO) activity and cytokines production including TNF-α and IL-6 (Zhang et al., 2010b)
Atherosclerosis	 Rhubarb (Dahuang)	Rhubarb were extracted by water	Atherosclerotic animal model (50 mg/kg/day)	Inhibits toll-like receptor (TLR)-2, TLR-4 and NF-κB mRNA and protein expressions (Liu et al., 2008b)
Atherosclerosis	 Paeonia lactiflora Pall (Bai shao)	Total glucosides of paeony (TGP) capsules: paeoniflorin (40 %),hydroxy-paeoniflorin (10 %) and other (50 %)	Vitamin D and cholesterol induced atherosclerosis model in rats (120 or 240 mg/kg)	Inhibits the serum level of inflammatory cytokines (IL-6, and TNF-α) (Li et al., 2011a)
Chronic vascular inflammation	 Ginkgo biloba (Yin xing)	 Ginkgolide B	Oxidized low-density lipoprotein (ox-LDL) stimulated human umbilical vein endothelial cells (HUVECs) (0.1-0.3 mg/mL)	Reduces intercellular adhesion molecule-1 (ICAM-1) expression, NF-κB signaling and inhibiting reactive oxygen species (ROS) generation (Li et al., 2009)
Atherosclerosis	 Glycyrrhizae glabra (Gan cao)	 Glycyrrhetinic acid	TNF-T-activated human umbilical vein endothelial cells (HUVEC) (50 μM)	Inhibits ICAM-1 expression, leading to a decrease in adherent monocytes (THP-1) to HUVEC by inhibition of TNF-α-activated JNK/c-Jun and NF-κB signaling pathways (Chang et al., 2010)
Vascular endothelial lesion	 Ginseng (Ren shen)	 Gnsenoside	L-methionine (3%) induced SD male rats (0.8 mg/kg/day)	Decreases iNOS and COX-2 expression (Li et al., 2008)

Group of diseases (target organ)	Chinese herbs		Experimental models Studied type (Dose)	Mechanism(s) of action (refs)
Atherogenesis	 Panax notoginseng (Sanqi)	 Saponins	Zymosan (10 mg/kg) high-cholesterol diet induced chronic inflammation in rabbits (120 mg/kg/day by oral gavage)	Reduces monocyte chemoattactant protein-1 (MCP-)1 and NF-κB mRNA expressions and serum level of IL-6 (Liu et al., 2010b)
Atherosclerosis	 Monascus purpureus (Hong qu)	 Monacolin K	Angiotensin II (AngII)-induced apolipoprotein E-deficient (ApoE−/−) mice (200 mg/kg/day by oral gavage)	Increases of serum macrophage migration inhibitory factor (MIF) and reductions of serum total cholesterol, intercellular adhesion molecule- 1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), matrix metalloproteinase (MMP)-2 (Xie et al., 2011)
Pancreas disease				
1. Type 1 diabetes 2. Inflammatory responses and insulin resistance	 Berberis vulgaris (Fu niu hua) Rhizoma coptidis (Huang lian)	 Berberine	1. B and T cells were isolated from nonobese diabetic (NOD) mice (200 mg/kg) 2. Palmitate (PA) stimulated HepG2 cells (0.1-10 μM)	1-1. Decreases Th17 cytokine secretion and differentiation by activation of ERK1/2 and down-regulation of p-STAT3 and RORγt expression 1-2. Reduces Th1 cytokine secretion and differentiation by inhibition of p38 MAPK and JNK activation and down-regulation of STAT1 and STAT4 activities (Cui et al., 2009) 2. Inhibits IL-6, and TNF-α production, modifies of insulin receptor substrate-1 (IRS-1) and downstream Akt (Lou et al., 2010)
Diabetic nephropathy	 Astragali radix (Huangqi)	 Calycosin	Advanced glycation end products (AGEs) -induced macrophages infiltration in HUVECs (10^{-8} M)	Reduces macrophage migration and adhesion to endothelial cells by down-regulation of transforming growth factor-b1(TGF-β1), ICAM-1 and receptor for advanced glycation end products (RAGE) expressions; increase estrogen receptor expression and inhibits p-ERK1/2 and p-NF-κB expression (Xu et al., 2011)
Obesity-related metabolic disorders: diabetic insulin resistance hypertriglyceridemia	 Radix astragali (Huangqi)		a. Human THP-1 macrophages (5-10 μg/mL) b. LPS-induced mouse RAW-Blue macrophage (10-20 μg/mL) c. C57BL/KsJ db/db diabetic mice (2g/kg/day)	a and b. Reduced the secretion of pro-inflammatory cytokines (TNF-α, IL-6 and MCP-1) c. Decreases CD68 and F4/80 mRNA expression and pro-inflammatory cytokines (MCP-1, TNF-α and IL-6), and increases arginase I in epididymal adipose tissue (Hoo et al., 2010)
Diabetic complications : foot ulcer	 Radix rehmanniae (Di huang)	1. Radix rehmanniae (RR) extract 2. 2-herb formula (NF3) was extracted from radix astragali (RA) and RR	1-a. Streptozotocin (STZ) -induced diabetic in rats 1-b. Carrageenan-induced inflammation in rats (1.85 mg/kg) 2. Streptozotocin (STZ) -induced diabetic in rats (0.98 g/kg)	1. Enhances vascular endothelial growth factor (VEGF) expression (Lau et al., 2009) 2. Reduction of wound area and LPS-induced NO production, stimulation of human fibroblast cells (Hs27) proliferation and promotion of HUVEC cell migration and tube formation (Tam et al., 2011)
Intestinal disease				
Colon inflammation	 Rubia cordifolia (Qian cao)	 Mollugin	a. TNF-α-induced HT-29 human colon epithelial cells b. TNF-α-induced attachment of U937 monocytic cells to HT-29 cells (20 μM)	a. Inhibits MCP-1 and IL-8, and ICAM-1 mRNA expression by blocking NF-κB activation b. Suppress TNF-Ŭ-induced U937 monocytic cell adhesion to HT-29 colonic epithelial cells (Kim et al., 2009)
Colon inflammation	 Sophora flavescens (Kushen)	 Matrine	LPS-stimulated second generation rat intestinal microvascular endothelial cells (RIMECs) (50 μg/mL)	Inhibits IL-6, IL-8, and soluble ICAM-1 production and improves NO-dependent vasomotion (Suo et al., 2009)

Group of diseases (target organ)	Chinese herbs		Experimental models Studied type (Dose)	Mechanism(s) of action (refs)
Ulcerative colitis	 **Fructus mume (Wumei)**	Berberine, hypaconitine and skimmianine from Fructus Mume pill (FMP)	a. Trinitrobenzene-sulfonic acid induced ulcerative colitis in rats b. Xylene-induced acute edema (6-27 mg/kg/day) c. Acetic acid-induced writhing (6-27 mg/kg/day) d. LPS-stimulated HT-29 cell (5-30 μM)	a. Inhibits TNF-α, lipopolysaccharide (LPS) binding protein (LBP) production and TLR-4 and NF-κB expression b and c. Relieving acetic acid-induced bowel pain and xylene-induced acute exudative edema d. Suppresses TNF-TTTLBP and PGE_2 levels (Zhang et al., 2011)
Immunoregulatory effects and colitis	 **Rheum tanguticum (Dahuang)**	Rhubarbs were extracted the polysaccharides-enriched fractions	Trinitrobenzene-sulfonic acid (TNBS)-induced colitis in rats (200 mg/kg/day)	Decreases TLR-4 activation and promoted the balance of Th1 and Th2 polarization, inhibited NF-κB activity. (Liu et al., 2009a)
Immunoregulatory effects and colitis	 **Sophora (Huai)**	 **Oxymatrine**	TNBS-induced colitis in rats (63 mg/kg/day)	Regulating the unbalance of Th1 and Th2 cytokines secretion via decreases IL-2 level and increases IL-10 level and NF-κB expression (Fan et al., 2008)
Pulmonary diseases				
Chronic allergic inflammation and asthma	 **Cordyceps (Dongchongcao)**	Cordyceps extract	Peripheral blood mononuclear cells (PBMCs) (10-20 μg/mL)	Inhibits the proliferation and differentiation of Th2 cells and reduce IL-4 and GATA-3 expression and increasing the content of IL-10 and expression forkhead/winged-helix transcription factor-3 (Foxp3) (Sun et al., 2010)
Allergic diseases and asthma	 **Vitex rotundifolia (Dan ye man jing)**	*Vitex rotundifolia* was extracted by distilled water	TNF-α, IL-4 and IL-1β stimulated A549 human alveolar epithelial cells (0.1-1 μg/mL)	Suppresses eotaxin secretion, eosinophil migration and down-regulated inflammation and cell adhesion-related genes (ICAM, VCAM, IL-8, NOS 2A and IL-5RA) by mitogen-activated protein kinase pathway (Sohn et al., 2009)
Airway inflammation	 **Viscum coloratum (Hujisheng)**	Partially purified extract (PPE-SVC) and viscolin were extracted from *Viscum coloratum* Nakai	Ovalbumin (OVA)-sensitized mice (5 mg/kg)	Suppresses airway hyperresponsiveness (AHR) and eosinophil infiltration of the lungs via reducing levels of chemokine (C-C motif) ligand (CCL) (CCL11 and CCL24), IgE and Th2-associated cytokines (IL-5) in bronchoalveolar lavage fluid (BALF) (Shen et al., 2011)
Lung inflammation	 **Eriobotrya japonica (Pi pa)**	 **Ursolic acid**	LPS-stimulated A549 cells (50 μg/mL)	Inhibites IL-8 production, NF-κB activation, and iNOS mRNA Expression (Lee et al., 2008)
Acute lung injury Lung inflammation	 **Tripterygium wilfordii (Lei gong teng)**	 **Triptolide**	a. Gq-coupled tachykinin 1 receptor with substance P or TNF- stimulated A549 cells b. Chlorine-exposed mice ($1.4\text{-}2.3x10^{-8}$ M or 12.5 mg/mL)	a. Inhibits IL-8 production and NF-κB activation b. Inhibits neutrophilic inflammation and the production of CXC chemokine KC (Cxcl1) (Hoyle et al., 2010)
Lung inflammation	 **ASHMI**	*Ganoderma lucidum*, Radix *Sophorae flavescenti*, Radix *Glycyrrhiza*	OVA or concanavalin A (ConA)-sensitized and challenged mice (10 mg/day)	Reduces levels of IgE and the Th2 cytokines(IL-4, IL-5, and IL-13) in lung and splenocyte cultures and increases IFN-γ secretion (Busse et al., 2010)
Pneumonia	 **Magnolia officinalis (Houpu)**	Polyphenol rich extract from *M. officinalis* bark (MPE)	Influenza virus A (IVA)-infected mice (10-20 mg/kg)	Reduces levels of serum NO, IL-6 and TNF-α, inhibits pneumonia and decreases lung viral titers through downregulation of NF-κB and TLR3 protein expressions in the lung tissue (Wu et al., 2011)

Group of diseases (target organ)	Chinese herbs		Experimental models Studied type (Dose)	Mechanism(s) of action (refs)
Lung inflammation	 Baicalin (Huangqin)	 Baicalin	Pneumocystis carinii infected rats (100-400 mg/kg/day)	Decreases the contents of TNF-α and soluble ICAM-1, and alleviate inflammation in lung tissues (Zhou and Zhou, 2009)
Joint diseases				
Arthritis	 Arisaema rhizomatum (Xue li jian)	Petroleum ether (PE), ethyl acetate (EE) n-butyl alcohol (n-BE) and water (WE) were extracted from ARCF rhizome	Type II bovine collagen (CII) -induced BALB/c mice (ME 130, 261, 522 mg/kg; EE 10.2, 20.4, 40.8 mg/kg; n-BE 52, 104, 208 mg/kg)	Suppresses paws and joints swelling and reduced the spleen indexes and reduces serum levels of inflammatory cytokines TNF-α, IL-1β, IL-6, IL-33 and rheumatoid factor (RF) (Chunxia et al., 2011)
Septic arthritis	 Epimedium pubescens (Yinyanghuo)	 Icariin	LPS-simulate chondrocytes (0.056-7.7 %)	Increases chondrocytes viability and extracellular matrix synthesis through inhibition of NO production, iNO, COX-2 and matrix metalloproteinase (MMP)–1, MMP-3, and MMP-13 expressions (Liu et al., 2010a)
Arthritis	 Erycibe obtusifolia Benth (Ding gong teng)	 Scopolin	Adjuvant-induced rats (50-100 mg/kg)	Inhibits paw swelling and articular index scores, and reduces IL-6, VEGF and fibroblast growth factor (FGF-2) expressions in rat synovial tissues (Pan et al., 2009b)
Arthritis Synovial inflammation	 Siegesbeckiae (Xi xian cao)	 Kirenol	Type II collagen-induced wistar rats (1-4 mg/kg)	Up-regulates nuclear Annexin-1expression and inhibits NF-κB activity in synovium, reduces IL-1β level and thereby depresse paw swelling (Wang et al., 2011)
Pain	 Pogostemon cablin (Guanghuoxiang)	*Pogostemon cablin* (PC) was extracted with methanol	a. Acetic acid-induced writhing response b. Formalin-induced paw licking c. γ-carrageenan (Carr)-induced mice paw edema (0.5-1.0 g/kg)	Decreases malondialdehyde (MDA) level, COX-2 and TNF-α activities by increasing the activities of anti-oxidant enzymes, such as superoxide dismutase (SOD), glutathione peroxidase (GPx) and glutathione reductase (GRx) (Lu et al., 2009b)
Pain	 Pterocephalus hookeri (Yi shou cao)	*Pterocephalus hookeri* (C.B. Clarke) was extracted with ethanol and aqueous	a. λ-carrageenan (Carr)-induced mice paw edema b. Cotton pellet-induced granuloma formation in rats c. Acetic acid-induced mice d. Xylene-induced ear edema (1-4 g/kg)	Increases the hot-plate pain threshold and reduced writhing response, rat paw edema perimeter, vascular permeability and granuloma weight (Zhang et al., 2009)
Pain Rheumatoid arthritis	 Ramulus mori (Sang zhi)	 *cis*-mulberroside A	a. Acetic acid-induced pain and Evans blue leakage in mice b. Carrageenan-induced mouse paw edema (25 and 50 mg/kg) c. LPS-stimulated RAW264.7 cells (25-50 (g/mL)	Inhibits pain, Evans blue leakage, paw edema, NO production and iNOS expression (Zhang and Shi, 2010)
Pain	 Zanthoxylum armatum (Zhu ye jiao)	Eudesmin, horsfieldin, fargesin, kobusin, sesamin, asarinin, planispine A, and pinoresinol-di-3,3-dimethylallyl	a. Acetic acid-induced mice b. Formalin induced mice c. Xylene-induced mice (100 and 800 mg/kg)	Decreases writhing numbers, licking times and ear swelling (Guo et al., 2011)
Pain Edema	 Saussurea involucrata (Xuelianhua)		a. Carrageenan-induced rats b. Xylene-induced mice c. Acetic acid-induced and d. Hot-plate test model (400 mg/kg)	Inhibits paw edema, ear edema, writhing and pain (Yi et al., 2010)

Group of diseases (target organ)	Chinese herbs		Experimental models Studied type (Dose)	Mechanism(s) of action (refs)
Pain Edema	 Celandine (Bai qu cai)	 Chelerythrine	a. Xylene-induced ear edema b. Formaldehyde-induced rats c. Acetic acid-induced mice d. LPS-stimulated peritoneal macrophages (1-5 mg/kg or 0.0001-0.1 μg/mL)	Inhibits writhing response, ear swelling and paw edema and decreases PGE production and COX-2 expression (Niu et al., 2011)
Pain Edema	 Alstonia scholaris (Dengtaishushu)	16-formyl-5α-methoxystrictamine, picralinal and tubotaiwine were extracted with ethanol from *Alstonia scholaris*	a. Acetic acid-induced mice b. Hot-plate and formalin tests in mice. c. Xylene-induced and mice d. Carrageenan-induced air pouch formation in mice (50-100 mg/kg)	Reduces writhing response, ear edema, NO, PGE2 and MDA, COX-1, COX-2 and 5-lipoxygenase (5-LOX) levels, and increases SOD activity (Shang et al., 2010)
Pain Edema	 Myrica rubra (Yangmei)	 Myricetin	a. Xylene, acetic acid and carrageenan-induced models b. Leukocyte migration assay c. Cotton pellet granuloma models (35 mg/kg)	Decreases ear edema, vascular permeability, paw edema, MDA level, leukocyte count and granuloma tissue formation by increases the serum level of SOD (Wang et al., 2010)
Pain Edema Osteoarthritis	 Murraya exotica (Jiulixiang)	Dried leaves of *M. exotica*. was extracted with ethanol	a. Acetic acid, hot-plate, carrageena and xylene -induced models b. Rat knee osteoarthritis model (Ethanol 70% extracts)	Decreases writhing response, paw edema, ear swelling, iNOS activity, IL-1β and TNF-α contents, and increases SOD activity and hot-plate pain latency (Wu et al., 2010)
Pain	 Oxytropis falcate (Lian xing ji dou)	 2′, 4′-dihydroxy-chalcone	a. Acetic acid-induced writhing response b. Complete Freund's adjuvant (CFA)-induced rats c. Thermally induced mice d. Xylene-induced ear edema (90.6 mg/kg)	Reduces ear edema and writhing (Chen et al., 2011)
Cutaneous diseases				
Skin inflammation	 Chrysanthemum indicum linne (Yeju)	*Chrysanthemum indicum Linne* (CIE) was extracted with 70% ethanol	12-O-tetradecanoyl-phorbol-13-acetate (TPA)-induced mouse ear edema (200 mg/kg)	Reduces skin thickness and tissue weight, inflammatory cytokine production (IL-1β and TNF-α), neutrophil-mediated myeloperoxidase (MPO) activity, and various histopathological indicators (Lee et al., 2009a)
Skin inflammation	 Asparagus cochinchinensis (Tiandong)	*Asparagus cochinchinensis* Merrill (ACE) was extracted with 70% ethanol	a. TPA-induced mouse ear edema (200 mg/kg) b. Acetic acid-induced mice (200 mg/kg)	Reduces skin thickness and tissue weight, inflammatory cytokine production (IL-1β and TNF-α), neutrophil-mediated MPO activity, vascular permeability and various histopathological indicators (Lee et al., 2009b)
Liver disease				
Alcoholic fatty liver disease (NAFLD)	 Keishibukuryogan (gui-zhi-fu-ling-wan)	*Cinnamomum cassia* blume, *Paeonia lactiflora* Pallas, *Prunus persica* Batsch, *Poria cocos* Wolf and *Paeonia suffruticosa* Andrews	NASH animal model and patients (Cinnamomi cortex 3 g Paeoniae radix Pallas 3 g Persicae semen Batsch 3 g Hoelen 3 g Moutan cortex 3 g)	Decreases liver injury and blood cholesterol (Fujimoto et al., 2010)
Non-alcoholic steatohepatitis (NASH)	Qu Yu Hua Tan Tong Luo decoction (QYHTTLD)		NASH patients (Radix Bupleuri 10 g Radix Scutellariae 12 g Rhizoma Pinelliae 10 g Radix Codonopsis Pilosulae 30 g, Radix Glycyrrhizae Praeparata 6g Fructus Ziziphi Jujubae 9 g, Rhizoma Polygoni Cuspidati 30 g, Radix Morindae Officinalis 8 g, Herba Hedyotis Diffusae 30 g)	Decreases IL-8, TNF-α and MDA levels and increases SOD activity (Zhang et al., 2008)

Abbreviations

TCM	traditional Chinese medicine
NF-κB	nuclear factor-κB
TNF-α	tumor necrosis factor-α
CCL	chemokine (C-C motif) ligand
iNOS	inducible nitric oxide synthase
COX2	cyclooxygenase 2
RO/NS	reactive oxygen/nitrogen species
IL	interleukins
LPS	lipopolysaccharide
PGE_2	prostaglandin E_2
NO	nitric oxide
IFN-γ	interferon-γ
MAPK	mitogen-activated protein kinase
PKC	protein kinase C
AP-1	activator protein 1
HIF-1α	hypoxia-inducible factor-1α
CNS	central nervous system
TGP	otal glucosides of peony
JNK	c-Jun N-terminal kinases
MEK3/6	MAPK extracellular signal-regulated kinases (ERK) kinase3/6
CVD	cardiovascular disease
MPO	myeloperoxidase
ox-LDL	oxidized low density lipoprotein
VCAM-1	vascular cell adhesion molecule-1
ICAM-1	intracellular adhesion molecule-1
MCP-1	monocyte chemoattractant protein-1
MMPs	matrix metalloproteinases
HUVEC	human umbilical vein endothelial cells
MIF	migration inhibitory factor
NOD	nonobese diabetic
RORγt	etinoic acid-related orphan receptor γt
AGEs	advanced glycation end products
TGF-β1	transforming growth factor-β1
RAGE	receptor for advanced glycation end products
VEGF	vascular endothelial growth factor
IBD	inflammatory bowel disease
UC	ulcerative colitis
ECs	endothelial cells
TNBS	2,4,6-trinitrobenzene sulfonic acid
AHR	airway hyperresponsiveness
OVA	ovalbumin
TLR	Toll like receptor
IVA	influenza virus A
RA	Rheumatoid arthritis
RF	rheumatoid factor
FGF-2	fibroblast growth factor
CFA	complete Freund's adjuvant
CIE	*Chrysanthemum indicum*
ACE	*Asparagus cochinchinensis* Merrill extract
TPA	12-O-tetradecanoyl-phorbol-13-acetate
NASH	non-alcoholic steatohepatitis
TGs	triglycerides
SOD	superoxide dismutase
GPx	glutathione peroxidase
GRx	glutathione reductase

References

Bae, H., Kim, H.J., Shin, M., Lee, H., Yin, C.S., Ra, J., Kim, J., 2010. Inhibitory effect of Agrimoniae Herba on lipopolysaccharide-induced nitric oxide and proinflammatory cytokine production in BV2 microglial cells. Neurological Research 32, 53-57.

Bouguen, G., Chevaux, J.B., Peyrin-Biroulet, L., 2011. Recent advances in cytokines: therapeutic implications for inflammatory bowel diseases. World Journal of Gastroenterology 17, 547-556.

Britschgi, M., Wyss-Coray, T., 2007. Immune cells may fend off Alzheimer disease. Nature Medicine 13, 408-409.

Busse, P.J., Schofield, B., Birmingham, N., Yang, N., Wen, M.C., Zhang, T., Srivastava, K., Li, X.M., 2010. The traditional Chinese herbal formula ASHMI inhibits allergic lung inflammation in antigen-sensitized and antigen-challenged aged mice. Annals of Allergy, Asthma and Immunology 104, 236-246.

Busse, W.W., Rosenwasser, L.J., 2003. Mechanisms of asthma. Journal of Allergy and Clinical Immunology 111, S799-S804.

Chang, Y.L., Chen, C.L., Kuo, C.L., Chen, B.C., You, J.S., 2010. Glycyrrhetinic acid inhibits ICAM-1 expression via blocking JNK and NF-kappaB pathways in TNF-alpha-activated endothelial cells. Acta Pharmacologica Sinica 31, 546-553.

Chen, Z.P., Qu, M.M., Chen, H.X., Liu,D., Xiao, Y.Y., Chen, J., Lu, T.L., Cai, B.C., 2011. The studies of anti-inflammatory and analgesic activities and pharmacokinetics of Oxytropis falcate Bunge extraction after transdermal administration in rats. Fitoterapia 82, 426-433.

Chunxia, C., Peng, Z., Huifang, P., Hanli, R., Zehua, H., Jizhou, W., 2011. Extracts of Arisaema rhizomatum C.E.C. Fischer attenuate inflammatory response on collagen-induced arthritis in BALB/c mice. Journal of Ethnopharmacology 133, 573-582.

Ci, X., Ren, R., Xu, K., Li, H., Yu, Q., Song, Y., Wang, D., Li, R., Deng, X., 2010. Schisantherin A exhibits anti-inflammatory properties by down-regulating NF-kappaB and MAPK signaling pathways in lipopolysaccharide-treated RAW 264.7 cells. Inflammation 33, 126-136.

Coussens, L.M., Werb, Z., 2002. Inflammation and cancer. Nature 420, 860-867.

Cui, G., Qin, X., Zhang, Y., Gong, Z., Ge, B., Zang, Y.Q., 2009. Berberine differentially modulates the activities of ERK, p38 MAPK, and JNK to suppress Th17 and Th1 T cell differentiation in type 1 diabetic mice. Journal of Biological Chemistry 284, 28420-28429.

Dudhgaonkar, S., Thyagarajan, A., Sliva, D., 2009. Suppression of the inflammatory response by triterpenes isolated from the mushroom Ganoderma lucidum. International Immunopharmacology 9, 1272-1280.

Dugasani, S., Pichika, M.R., Nadarajah, V.D., Balijepalli, M.K., Tandra, S., Korlakunta, J.N., 2010. Comparative antioxidant and anti-inflammatory effects of [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol. Journal of Ethnopharmacology 127, 515-520.

Fan, H., Chen, R., Shen, L., Lv, J., Xiong, P., Shou, Z., Zhuang, X., 2008. Oxymatrine improves TNBS-induced colitis in rats by inhibiting the expression of NF-kappaB p65. Journal of Huazhong University of Science and Technology [Medical Sciences] 28, 415-420.

Ferre, N., Claria, J., 2006. New insights into the regulation of liver inflammation and oxidative stress. Mini reviews in medicinal chemistry 6, 1321-1330.

Forrester, J.S., Bick-Forrester, J., 2005. Persistence of inflammatory cytokines cause a spectrum of chronic progressive diseases: implications for therapy. Medical Hypotheses 65, 227-231.

Fujimoto, M., Tsuneyama, K., Kinoshita, H., Goto, H., Takano, Y., Selmi, C., Keen, C.L., Gershwin, M.E., Shimada, Y., 2010. The traditional Japanese formula keishibukuryogan reduces liver injury and inflammation in patients with nonalcoholic fatty liver disease. Annals of the NEW YORK Academy of Sciences 1190, 151-158.

Guo, T., Deng, Y.X., Xie, H., Yao, C.Y., Cai, C.C., Pan, S.L., Wang, Y.L., 2011. Antinociceptive and anti-inflammatory activities

of ethyl acetate fraction from Zanthoxylum armatum in mice. Fitoterapia 82, 347-351.

Handschin, C., Spiegelman, B.M., 2008. The role of exercise and PGC1alpha in inflammation and chronic disease. Nature 454, 463-469.

Ho, S.C., Lin, C.C., 2008. Investigation of heat treating conditions for enhancing the anti-inflammatory activity of citrus fruit (Citrus reticulata) peels. Journal of Agricultural and Food Chemistry 56, 7976-7982.

Hoo, R.L., Wong, J.Y., Qiao, C., Xu, A., Xu, H., Lam, K.S., 2010. The effective fraction isolated from Radix Astragali alleviates glucose intolerance, insulin resistance and hypertriglyceridemia in db/db diabetic mice through its anti-inflammatory activity. Nutrition and Metabolism (Lond) 7, 67.

Hotamisligil, G.S., 2006. Inflammation and metabolic disorders. Nature 444, 860-867.

Hoyle, G.W., Hoyle, C.I., Chen, J., Chang, W., Williams, R.W., Rando, R.J., 2010. Identification of triptolide, a natural diterpenoid compound, as an inhibitor of lung inflammation. American Journal of Physiology - Lung Cellular and Molecular Physiology 298, 830-836.

Hua, Q., Zhu, X.L., Li, P.T., Liu, Y., Zhang, N., Xu, Y., Jia, X., 2009. The inhibitory effects of cholalic acid and hyodeoxycholalic acid on the expression of TNFalpha and IL-1beta after cerebral ischemia in rats. Archives of Pharmacal Research 32, 65-73.

Huang, D., Liu, M., Yan, X., 2011. Effects of total glucosides of peony on expression of inflammatory cytokines and phosphorylated MAPK signal molecules in hippocampus induced by fibrillar Abeta42. Zhongguo Zhong.Yao Za Zhi 36, 795-800.

Hwang, P.A., Chien, S.Y., Chan, Y.L., Lu, M.K., Wu, C.H., Kong, Z.L., Wu, C.J., 2011. Inhibition of Lipopolysaccharide (LPS)-induced inflammatory responses by Sargassum hemiphyllum sulfated polysaccharide extract in RAW 264.7 macrophage cells. Journal of Agricultural and Food Chemistry 59, 2062-2068.

Ichikawa, H., Wang, X., Konishi, T., 2003. Role of component herbs in antioxidant activity of shengmai san--a traditional Chinese medicine formula preventing cerebral oxidative damage in rat. The American Journal of Chinese Medicine 31, 509-521.

Iwamoto, I., 2003. Molecular mechanisms of allergic airway inflammation in asthma. Nihon Kokyuki.Gakkai Zasshi 41, 600-605.

Izumimoto, N., Kawakami, A., 2011. Inflammation in atherosclerosis. Nihon Rinsho 69, 2-5.

Jose, L.A., Garrote, J.A., Arranz, E., 2006. Cytokines in the pathogenesis of inflammatory bowel diseases. Medicina Clinica (Barc.) 127, 145-152.

Kalousova, M., Fialova, L., Skrha, J., Zima, T., Soukupova, J., Malbohan, I.M., Stipek, S., 2004. Oxidative stress, inflammation and autoimmune reaction in type 1 and type 2 diabetes mellitus. Prague Medical Report 105, 21-28.

Khatami, M., 2009. Inflammation, aging, and cancer: tumoricidal versus tumorigenesis of immunity: a common denominator mapping chronic diseases. Cell Biochemistry and Biophysics 55, 55-79.

Kim, K.J., Lee, J.S., Kwak, M.K., Choi, H.G., Yong, C.S., Kim, J.A., Lee, Y.R., Lyoo, W.S., Park, Y.J., 2009. Anti-inflammatory action of mollugin and its synthetic derivatives in HT-29 human colonic epithelial cells is mediated through inhibition of NF-kappaB activation. European Journal of Pharmacology 622, 52-57.

Lau, T.W., Lam, F.F., Lau, K.M., Chan, Y.W., Lee, K.M., Sahota, D.S., Ho, Y.Y., Fung, K.P., Leung, P.C., Lau, C.B., 2009. Pharmacological investigation on the wound healing effects of Radix Rehmanniae in an animal model of diabetic foot ulcer. Journal of Ethnopharmacology 123, 155-162.

Lee, C.H., Chen, J.C., Hsiang, C.Y., Wu, S.L., Wu, H.C., Ho, T.Y., 2007. Berberine suppresses inflammatory agents-induced interleukin-1beta and tumor necrosis factor-alpha productions via the inhibition of IkappaB degradation in human lung cells. Pharmacological Research 56, 193-201.

Lee, C.H., Wu, S.L., Chen, J.C., Li, C.C., Lo, H.Y., Cheng, W.Y., Lin, J.G., Chang, Y.H., Hsiang, C.Y., Ho, T.Y., 2008. Eriobotrya japonica leaf and its triterpenes inhibited lipopolysaccharide-induced cytokines and inducible enzyme production via the nuclear factor-kappaB signaling pathway in lung epithelial cells. The American Journal of Chinese Medicine 36, 1185-1198.

Lee, D.Y., Choi, G., Yoon, T., Cheon, M.S., Choo, B.K., Kim, H.K., 2009a. Anti-inflammatory activity of Chrysanthemum indicum extract in acute and chronic cutaneous inflammation. Journal of Ethnopharmacology 123, 149-154.

Lee, D.Y., Choo, B.K., Yoon, T., Cheon, M.S., Lee, H.W., Lee, A.Y., Kim, H.K., 2009b. Anti-inflammatory effects of Asparagus cochinchinensis extract in acute and chronic cutaneous inflammation. Journal of Ethnopharmacology 121, 28-34.

Lee, T.Y., Lee, K.C., Chen, S.Y., Chang, H.H., 2009c. 6-Gingerol inhibits ROS and iNOS through the suppression of PKC-alpha and NF-kappaB pathways in lipopolysaccharide-stimulated mouse macrophages. Biochemical and Biophysical Research Communications 382, 134-139.

Leff, L., 2006. Emerging new therapies in rheumatoid arthritis: what's next for the patient? Journal of infusion nursing 29, 326-337.

Levin, M.E., 2002. Management of the diabetic foot: preventing amputation. Southern Medical Journal 95, 10-20.

Li, J., Chen, C.X., Shen, Y.H., 2011a. Effects of total glucosides from paeony (Paeonia lactiflora Pall) roots on experimental atherosclerosis in rats. Journal of Ethnopharmacology 135, 469-475.

Li, R., Chen, B., Wu, W., Bao, L., Li, J., Qi, R., 2009. Ginkgolide B suppresses intercellular adhesion molecule-1 expression via blocking nuclear factor-kappaB activation in human vascular endothelial cells stimulated by oxidized low-density lipoprotein. Journal of Pharmacological Sciences 110, 362-369.

Li, W., Zhou, P., Zhang, Y., He, L., 2011b. Houttuynia cordata, a novel and selective COX-2 inhibitor with anti-inflammatory activity. Journal of Ethnopharmacology 133, 922-927.

Li, Y.N., Wu, Y.L., Jia, Z.H., Qi, J.S., 2008. Interaction between COX-2 and iNOS aggravates vascular lesion and antagonistic effect of ginsenoside. Journal of Ethnopharmacology 119, 305-311.

Libby, P., 2006. Inflammation and cardiovascular disease mechanisms. The American Journal of Clinical Nutrition 83, 456-460.

Libby, P., Theroux, P., 2005. Pathophysiology of coronary artery disease. Circulation 111, 3481-3488.

Lim, H., Lee, J.G., Lee, S.H., Kim, Y.S., Kim, H.P., 2008. Anti-inflammatory activity of phylligenin, a lignan from the fruits of Forsythia koreana, and its cellular mechanism of action. Journal of Ethnopharmacology 118, 113-117.

Lin, Q.Y., Jin, L.J., Cao, Z.H., Xu, Y.P., 2008. Inhibition of inducible nitric oxide synthase by Acanthopanax senticosus extract in RAW264.7 macrophages. Journal of Ethnopharmacology 118, 231-236.

Lin, W.C., Lin, J.Y., 2011. Five bitter compounds display different anti-inflammatory effects through modulating cytokine secretion using mouse primary splenocytes *in vitro*. Journal of Agricultural and Food Chemistry 59, 184-192.

Ling, S., Zhang, H., Zhang, D., Zhang, L., Bian, K., 2010. Characterizing effects of solvent specific morus alba components on rat platelet aggregation, vascular tension and macrophage nitrite production. Zhongguo Zhong.Yao Za Zhi 35, 3024-3028.

Liu, J., Wang, Z.T., Ge, B.X., 2008a. Andrograpanin, isolated from Andrographis paniculata, exhibits anti-inflammatory property in lipopolysaccharide-induced macrophage cells through down-regulating the p38 MAPKs signaling pathways. International Immunopharmacology 8, 951-958.

Liu, L., Yuan, S., Long, Y., Guo, Z., Sun, Y., Li, Y., Niu, Y., Li, C., Mei, Q., 2009a. Immunomodulation of Rheum tanguticum polysaccharide (RTP) on the immunosuppressive effects of dexamethasone (DEX) on the treatment of colitis in rats induced by 2,4,6-trinitrobenzene sulfonic acid. International Immunopharmacology 9, 1568-1577.

Liu, M.H., Sun, J.S., Tsai, S.W., Sheu, S.Y., Chen, M.H., 2010a. Icariin protects murine chondrocytes from lipopolysaccharide-

induced inflammatory responses and extracellular matrix degradation. Nutrition Research 30, 57-65.

Liu, Y., Yan, F., Liu, Y., Zhang, C., Yu, H., Zhang, Y., Zhao, Y., 2008b. Aqueous extract of rhubarb stabilizes vulnerable atherosclerotic plaques due to depression of inflammation and lipid accumulation. phytotherapy research 22, 935-942.

Liu, Y., Zhang, H.G., Jia, Y., Li, X.H., 2010b. Panax notoginseng saponins attenuate atherogenesis accelerated by zymosan in rabbits. Biological & Pharmaceutical Bulletin 33, 1324-1330.

Liu, Y.N., Pan, S.L., Liao, C.H., Huang, D.Y., Guh, J.H., Peng, C.Y., Chang, Y.L., Teng, C.M., 2009b. Evodiamine represses hypoxia-induced inflammatory proteins expression and hypoxia-inducible factor 1alpha accumulation in RAW264.7. Shock 32, 263-269.

Lou, T., Zhang, Z., Xi, Z., Liu, K., Li, L., Liu, B., Huang, F., 2010. Berberine Inhibits Inflammatory Response and Ameliorates Insulin Resistance in Hepatocytes. Inflammation 26,

Lu, L.M., Chen, X., Xu, J.T., 2009a. Determination methods for inspection of the complexion in traditional Chinese medicine: a review. Zhong.Xi.Yi.Jie.He.Xue.Bao 7, 701-705.

Lu, T.C., Liao, J.C., Huang, T.H., Lin, Y.C., Liu, C.Y., Chiu, Y.J., Peng, W.H., 2009b. Analgesic and Anti-Inflammatory Activities of the Methanol Extract from Pogostemon cablin. Evidence-based Complementary and Alternative Medicine 2011, 1-9.

Luo, Y., Liu, M., Yao, X., Xia, Y., Dai, Y., Chou, G., Wang, Z., 2009. Total alkaloids from Radix Linderae prevent the production of inflammatory mediators in lipopolysaccharide-stimulated RAW 264.7 cells by suppressing NF-kappaB and MAPKs activation. Cytokine 46, 104-110.

Mantovani, A., 2010. Molecular pathways linking inflammation and cancer. Current Molecular Medicine 10, 369-373.

Marrelli, A., Cipriani, P., Liakouli, V., Carubbi, F., Perricone, C., Perricone, R., Giacomelli, R., 2011. Angiogenesis in rheumatoid arthritis: A disease specific process or a common response to chronic inflammation? Autoimmunity Reviews 10, 595-598.

Mito, S., 2011. Curcumin ameliorates cardiac inflammation in rats with autoimmune myocarditis 34, 974-9.

Niu, X.F., Zhou, P., Li, W.F., Xu, H.B., 2011. Effects of chelerythrine, a specific inhibitor of cyclooxygenase-2, on acute inflammation in mice. Fitoterapia 82, 620-625.

Numerof, R.P., Dinarello, C.A., Asadullah, K., 2005. Cytokines as potential therapeutic targets for inflammatory skin diseases. European Cytokine Network 16, 101-103.

Or, T.C., Yang, C.L., Law, A.H., Li, J.C., Lau, A.S., 2011b. Isolation and identification of anti-inflammatory constituents from Ligusticum chuanxiong and their underlying mechanisms of action on microglia. Neuropharmacology 60, 823-831.

Or, T.C., Yang, C.L., Law, A.H., Li, J.C., Lau, A.S., 2011a. Isolation and identification of anti-inflammatory constituents from Ligusticum chuanxiong and their underlying mechanisms of action on microglia. Neuropharmacology 60, 823-831.

Packard, R.R., Libby, P., 2008. Inflammation in atherosclerosis: from vascular biology to biomarker discovery and risk prediction. Clinical Chemistry 54, 24-38.

Pan, C.H., Kim, E.S., Jung, S.H., Nho, C.W., Lee, J.K., 2008. Tectorigenin inhibits IFN-gamma/LPS-induced inflammatory responses in murine macrophage RAW 264.7 cells. Archives of Pharmacal Research 31, 1447-1456.

Pan, M.H., Lai, C.S., Dushenkov, S., Ho, C.T., 2009a. Modulation of inflammatory genes by natural dietary bioactive compounds. Journal of Agricultural and Food Chemistry 57, 4467-4477.

Pan, R., Dai, Y., Gao, X., Xia, Y., 2009b. Scopolin isolated from Erycibe obtusifolia Benth stems suppresses adjuvant-induced rat arthritis by inhibiting inflammation and angiogenesis. International Immunopharmacology 9, 859-869.

Pan, W., Liu, Y., Fang, Z., Zhu, X., Pan, W., Kwak, S., Yamamoto, Y., 2011. A compound belonging to traditional Chinese medicine improves nocturnal activity in Parkinson's disease. Sleep Medicine 12, 307-308.

Pari, L., Tewas, D., Eckel, J., 2008. Role of curcumin in health and disease. Archives of Physiology and Biochemistry 114, 127-149.

Rao, Y.K., Fang, S.H., Hsieh, S.C., Yeh, T.H., Tzeng, Y.M., 2009. The constituents of Anisomeles indica and their anti-inflammatory activities. Journal of Ethnopharmacology 121, 292-296.

Ren, Y., Song, C.S., Liu, X.H., Shi, Y., Gao, J.F., He, X.D., 1994. Experimental study on compatible application of heat-clearing and detoxifying drugs with blood circulation improving drugs. Zhongguo Zhong.Yao Za Zhi 19, 626-8, 640.

Ren, Z.H., Tong, Y.H., Xu, W., Ma,J., Chen, Y., 2010. Tanshinone II A attenuates inflammatory responses of rats with myocardial infarction by reducing MCP-1 expression. Phytomedicine 17, 212-218.

Rivest, S., 2009. Regulation of innate immune responses in the brain. Nature Reviews Immunology 9, 429-439.

Schmid-Hempel, P., 2005. Natural insect host-parasite systems show immune priming and specificity: puzzles to be solved. Bioessays 27, 1026-1034.

Schoneveld, A.H., Hoefer, I., Sluijter, J.P., Laman, J.D., de Kleijn, D.P., Pasterkamp, G., 2008. Atherosclerotic lesion development and Toll like receptor 2 and 4 responsiveness. Atherosclerosis 197, 95-104.

Shang, J.H., Cai, X.H., Feng, T., Zhao, Y.L., Wang, J.K., Zhang, L.Y., Yan, M., Luo, X.D., 2010. Pharmacological evaluation of Alstonia scholaris: anti-inflammatory and analgesic effects. Journal of Ethnopharmacology 129, 174-181.

Shen,J.J., Chiang, M.S., Kuo, M.L., Leu,Y.L., Hwang, T.L., Liou, C.J., Huang, W.C., 2011. Partially purified extract and viscolin from Viscum coloratum attenuate airway inflammation and eosinophil infiltration in ovalbumin-sensitized mice. Journal of Ethnopharmacology 135, 646-653.

Sohn, S.H., Ko, E., Oh, B.G., Kim, S.H., Kim, Y., Shin, M., Hong, M., Bae, H., 2009. Inhibition effects of Vitex rotundifolia on inflammatory gene expression in A549 human epithelial cells. Annals of Allergy, Asthma and Immunology 103, 152-159.

Su, Y.W., Chiou, W.F., Chao, S.H., Lee, M.H., Chen, C.C., Tsai, Y.C., 2011. Ligustilide prevents LPS-induced iNOS expression in RAW 264.7 macrophages by preventing ROS production and down-regulating the MAPK, NF-kappaB and AP-1 signaling pathways. International Immunopharmacology 11, 1166-1172

Sun, W., Yu, J., Shi, Y.M., Zhang, H., Wang, Y., Wu, B.B., 2010. Effects of Cordyceps extract on cytokines and transcription factors in peripheral blood mononuclear cells of asthmatic children during remission stage. Zhong.Xi.Yi.Jie.He.Xue.Bao 8, 341-346.

Suo, Z., Liu, Y., Ferreri, M., Zhang, T., Liu, Z., Mu, X., Han, B., 2009. Impact of matrine on inflammation related factors in rat intestinal microvascular endothelial cells.1. Journal of Ethnopharmacology 125, 404-409.

Tam, J.C., Lau, K.M., Liu, C.L., To, M.H., Kwok, H.F., Lai, K.K., Lau, C.P., Ko, C.H., Leung, P.C., Fung, K.P., Lau, C.B., 2011. The in vivo and *in vitro* diabetic wound healing effects of a 2-herb formula and its mechanisms of action. Journal of Ethnopharmacology 134, 831-838.

Tilg, H., Kaser, A., Moschen, A.R., 2006. How to modulate inflammatory cytokines in liver diseases. Liver International 26, 1029-1039.

Tsianos, E.V., Katsanos, K., 2009. Do we really understand what the immunological disturbances in inflammatory bowel disease mean? World Journal of Gastroenterology 15, 521-525.

Wang, S.J., Tong, Y., Lu, S., Yang, R., Liao, X., Xu, Y.F., Li, X., 2010. Anti-inflammatory activity of myricetin isolated from Myrica rubra Sieb. et Zucc. leaves. Planta Medica 76, 1492-1496.

Wang, Y., Kong, L., Lei, X., Hu, L., Zou, H., Welbeck, E., Bligh, S.W., Wang, Z., 2009. Comprehensive two-dimensional high-performance liquid chromatography system with immobilized liposome chromatography column and reversed-phase column for separation of complex traditional Chinese medicine Longdan Xiegan Decoction. Journal of Chromatography A 1216, 2185-2191.

Wang, Z.M., Zhu, S.G., Wu, Z.W., Lu, Y., Fu, H.Z., Qian, R.Q., 2011. Kirenol upregulates nuclear Annexin-1 which interacts with NF-kappaB to attenuate synovial inflammation of collagen-induced arthritis in rats. Journal of Ethnopharmacology 137, 774-782

Wu, L., Li, P., Wang, X., Zhuang, Z., Farzaneh, F., Xu, R., 2010. Evaluation of anti-inflammatory and antinociceptive activities of Murraya exotica. Pharmaceutical Biology 48, 1344-1353.

Wu, X.N., Yu, C.H., Cai, W., Hua, J., Li, S.Q., Wang, W., 2011. Protective effect of a polyphenolic rich extract from Magnolia officinalis bark on influenza virus-induced pneumonia in mice. Journal of Ethnopharmacology 134, 191-194.

Xie, W., Du, L., 2011. Diabetes is an inflammatory disease: evidence from traditional Chinese medicines. Diabetes, Obesity and Metabolism 13, 289-301.

Xie, X., Wang, Y., Zhang, S., Zhang, G., Xu, Y., Bi, H., Daugherty, A., Wang, J.A., 2011. Chinese red yeast rice attenuates the development of angiotensin II-induced abdominal aortic aneurysm and atherosclerosis. The Journal of Nutritional Biochemistry doi:10.1016/j.jnutbio.2011.02.011.

Xu, G., 2006. Treatment of reflux laryngopharyngitis with modified banxia xiexin tang (Pinellia decoction for draining the heart)--a report of 40 cases. Home - Journal of Traditional Chinese Medicine 26, 127-131.

Xu, Y., Feng, L., Wang, S., Zhu, Q., Zheng, Z., Xiang, P., He, B., Tang, D., 2011. Calycosin protects HUVECs from advanced glycation end products-induced macrophage infiltration. Journal of Ethnopharmacology 137, 359-370.

Yang, C.L., Chik, S.C., Li, J.C., Cheung, B.K., Lau,A.S. 2009. Identification of the bioactive constituent and its mechanisms of action in mediating the anti-inflammatory effects of black cohosh and related Cimicifuga species on human primary blood macrophages. Journal of Medicinal Chemistry . 52, 6707-6715.

Yarosh, D.B., Galvin, J.W., Nay, S.L., Pena, A.V., Canning, M.T., Brown, D.A., 2006. Anti-inflammatory activity in skin by biomimetic of Evodia rutaecarpa extract from traditional Chinese medicine. Journal of Dermatological Science 42, 13-21.

Yi, T., Zhao, Z.Z., Yu, Z.L., Chen, H.B., 2010. Comparison of the anti-inflammatory and anti-nociceptive effects of three medicinal plants known as "Snow Lotus" herb in traditional Uighur and Tibetan medicines. Journal of Ethnopharmacology 128, 405-411.

Zhang, D., Nie, X., Pan, H., Yu, L., Yang, X., Xu, J., Bian, K., 2010a. Study on effect of total saponins from Semen Nigellae on inflammatory mediators and ERK/MAPK pathway in stimulated macrophage. Zhongguo Zhong.Yao Za Zhi 35, 2594-2598.

Zhang, L., Hu, J.J., Lin, J.W., Fang, W.S., Du, G.H., 2009. Anti-inflammatory and analgesic effects of ethanol and aqueous extracts of Pterocephalus hookeri (C.B. Clarke) Hoeck. Journal of Ethnopharmacology 123, 510-514.

Zhang, M., Long, Y., Sun, Y., Wang, Y., Li, Q., Wu, H., Guo, Z., Li, Y., Niu, Y., Li, C., Liu, L., Mei, Q., 2011. Evidence for the complementary and synergistic effects of the three-alkaloid combination regimen containing berberine, hypaconitine and skimmianine on the ulcerative colitis rats induced by trinitrobenzene-sulfonic acid. European Journal of Pharmacology 651, 187-196.

Zhang, S.J., Chen, Z.X., Jiang, K.P., Cheng, Y.H., Gu, Y.L., 2008. The effect of QuYuHuaTanTongLuo Decoction on the non-alcoholic steatohepatitis. Complementary Therapies in Medicine 16, 192-198.

Zhang, Y., Wei, L., Sun, D., Cao, F., Gao, H., Zhao, L., Du, J., Li, Y., Wang, H., 2010b. Tanshinone IIA pretreatment protects myocardium against ischaemia/reperfusion injury through the phosphatidylinositol 3-kinase/Akt-dependent pathway in diabetic rats. Diabetes, Obesity and Metabolism 12, 316-322.

Zhang, Z., Shi, L., 2010. Anti-inflammatory and analgesic properties of cis-mulberroside A from Ramulus mori. Fitoterapia 81, 214-218.

Zhang, Z.L., Zuo, Y.M., Wang, Q.H., Xiao, H.B., Kuang, H.X., 2010c. Effects of Valeriana amurensis on the expressions of iNOS, COX-2 and IkappaCB-alpha in Alzheimer's disease model rat's brain. Zhong Yao Cai 33, 581-583.

Zhou, L., Zhou, B.Y., 2009. Influence of baicalin on TNF-alpha and soluble intercellular adhesion molecule-1 in rats infected with Pneumocystis carinii. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 27, 144-147.

Zhu, L.H., Bi, W., Qi, R.B. Wang, H.D., Lu, D.X., 2011b. Luteolin inhibits microglial inflammation and improves neuron survival against inflammation. International Journal of Neuroscience 121, 329-336.

Zhu, L.H., Bi, W., Qi, R.B. Wang, H.D., Lu, D.X., 2011a. Luteolin inhibits microglial inflammation and improves neuron survival against inflammation. International Journal of Neuroscience 121, 329-336.