



Anti-inflammatory and Antimicrobial Effects of Heat-clearing Chinese Herbs: A Current Review

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ABSTRACT

Inflammation is a normal immune response; but if the body's regulation of inflammation is dysfunctional, then it will have an adverse effect on the body. Although use of modern drugs for inflammation has a relieving effect, it is still unsatisfactory. Moreover, the emergence of drug-resistant strains and even new kinds of microorganisms is causing significant morbidity and mortality. Recently, more attention has been focused on herbal medicine to treat various diseases because of the ability of the herbs to affect multiple target signaling pathways and their multiple mechanisms of action. Thus, a large number of studies have reported on the anti-inflammatory and antimicrobial effects of the traditional Chinese herbs. Literature survey was performed by conducting systematic electronic search in PubMed, Science Direct, Google Scholar, and in books. This review has listed 11 heat-clearing Chinese herbs (HCCHs) including *Scutellaria baicalensis* (黃芩 Huáng Qín), *Coptis chinensis* (黃連 Huáng Lián), *Flos Lonicerae* (金銀花 Jīn Yīn Huā), *Forsythia suspensa* (連翹 Lián Qiào), *Isatidis Folium* (大青葉 Dà Qīn Yè), *Radix Isatidis* (板藍根 Bǎn Lán Gēn), *Viola yedoensis* (紫花地丁 Zǐ Huā Dì Dīng), *Pulsatilla Radix* (白頭翁 Bái Tóu Wēng), *Andrographis paniculata* (穿心蓮 Chuān Xīn Lián), *Houttuynia cordata* (魚腥草 Yú Xīng Cǎo), and *Patrinia Herba* (敗醬草 Bài Jiàng Cǎo), which have anti-inflammatory and antimicrobial effects, and has described their effects through different mechanisms of action and multiple targets. Their ability to affect multiple target signaling pathways and their potential mechanisms of action contributing to their anti-inflammatory and antimicrobial activity may be related to their action of removing heat and counteracting toxicity. Further studies are needed on the collection of HCCHs to know the detailed mechanism of action of herbs in this group for the assessment of effective drug.

Key words: Anti-inflammatory activity, Antimicrobial activity, Heat-clearing Chinese herbs, Traditional Chinese Medicine

INTRODUCTION

Inflammation is a part of the immune response that can prevent infection through production of pro-inflammatory cytokines and generation of inflammatory mediators in response to microbial products.^[1] Although inflammation is crucial to maintaining the health and integrity of an organism, when the inflammatory process is poorly controlled, it can cause massive tissue destruc-

tion and a series of chain reactions.^[2-4] The current treatment of inflammatory disorders involves extensive use of nonsteroidal anti-inflammatory drugs and corticosteroids. Although use of modern drugs for inflammation has a relieving effect, it is still unsatisfactory.^[5] Moreover, bacterial resistance to antibiotics and the emergence of new kinds of microorganisms are becoming an increasing problem all over the world, causing significant morbidity and mortality.^[6,7] In order to combat this problem, novel

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antibiotic and anti-inflammatory compounds need to be found which are both effective and safe.

Traditional Chinese Medicine (TCM) has been used in China over thousands of years for the prevention and treatment of various diseases.^[6,8,9] TCM uses yin–yang theory to explain the organizational structure, physiological functions, and pathological changes in the human body and to guide diagnosis and treatment of disease.^[5,10] Although yin and yang are contradictory in nature, they depend on each other for existence. Keeping balance between yin and yang is very important to maintain the healthy state of human body. TCM theory states that the occurrence of the disease depends on the interaction between zheng qi (nonpathogenic qi) and xie qi (pathogenic qi). The idea of disease is the struggle between pathogenic qi and nonpathogenic qi; in this struggle process, there will be changes between yin and yang. TCM holds that variation between the evil aspect and healthy trend determines the occurrence of disease. Therefore, in TCM, inflammatory and antimicrobial therapy lies in strengthening the healthy trend and dispelling the evil aspect in order to keep a balanced state between yin and yang.^[5,11]

Herbal medicine is one of the main components of TCM which has long been used for its multiple types of disease treatment. In recent times, it is making a rapid progress in scientific investigation and attracting great attention due to the good therapeutic effects and minimal side effects of the herbs.^[6,8,12] Chinese herbs used in the treatment of diseases are grouped into many categories. One of these is heat-clearing Chinese herbs (HCCHs). Herbs in this group are mostly cold in nature and can clear away heat, purge fire, dry dampness, cool blood, and relieve toxic material. Their main action is clearing away interior heat, and thus they are considered to be antipyretic.^[11,13] Because of all these properties, HCCHs may be effective in the treatment of inflammatory disease and microbial infection. This review tries to summarize the effect of HCCHs which have shown anti-inflammatory and antimicrobial activities and their mechanisms of action.

Scutellaria baicalensis (黃芩 Huáng Qín)

Scutellaria baicalensis is a species of flowering plant belonging to Lamiaceae family. It is a heat-clearing, phlegm-removing herb, traditionally used to cool heat, drain fire, clear damp-heat, stop bleeding, calm the fetus, and descend yang.^[11,13,14] The dry root part of *Sc. baicalensis* has many pharmacological effects including antipyretic, hepatoprotective, antihypertensive, diuretic, and antibiotic activities. It is mildly sedating and also used to treat dysentery and chronic hepatitis.^[6,7,14,15] *Sc. baicalensis* has distinct effects in the treatment of inflammatory diseases; it alleviates inflammation by decreasing the expression of interleukin (IL)-1b, IL-6, and IL-12, and the production of tumor necrosis factor (TNF)- α and soluble intercellular adhesion molecule-1 (ICAM-1).^[5,16] In Xie xin herbal decoction, huang qin, in combination with huang lian, inhibits nitric oxide (NO) production *in vitro* and *in vivo* in lipopolysaccharide (LPS)-stimulated RAW264.7 cells. Oroxylin A, which is a flavonoid found in dried root of *Sc. baicalensis*, has also shown good anti-inflammatory effect.^[17,18] Moreover, *Sc. baicalensis* has antibacterial effect against *Helicobacter pylori* as well as inhibits the growth of

Escherichia coli B, coagulase-negative staphylococci, and *Saccharomyces cerevisiae*.^[7,15]

Coptis chinensis (黃連 Huáng Lián)

Coptis chinensis belongs to Ranunculaceae family. Traditionally, it has been used to drain fire, detoxify and disinfect, stop bleeding, cure eczema, burns, and ulcer, and to descend yang.^[7,11,13,14,19] The main pharmacodynamic properties have long been recognized in the treatment of intestinal infections including acute gastroenteritis, cholera, and bacillary dysentery. It also used for treating various diseases including skin diseases, conjunctivitis, otitis, and hypertension.^[14,19,20] *C. chinensis* has been demonstrated to have anti-inflammatory effects through different mechanisms. It inhibits TNF-induced Nuclear factor-kappaB (NF- κ B) signaling in human keratinocytes by blocking the NF- κ B-dependent pathway. It also decreases Th17 cytokine secretion and differentiation by activation of extracellular signal-regulated protein kinases 1 and 2 (ERK1/2) and down-regulation of phosphorylated signal transducer and activator of transcription 3 (p-STAT3) and retinoic acid-related orphan receptor γ t (ROR γ t) expression. It also reduces Th1 cytokine secretion and differentiation by inhibition of protein 38 (p38) mitogen activated protein kinase (MAPK) and Jun N-terminal kinase (JNK) activation along with down-regulation of STAT1 and STAT4 activities.^[21,22] In combination with other herbs, *C. chinensis* exhibited a good anti-inflammatory effect; the ethanol extract from Zuojin Pill inhibited inducible nitric oxide synthase (iNOS), cyclooxygenase 2 (COX-2), IL-6, IL-1 β , and TNF- α expression by preventing the nuclear translocation of the NF- κ B p50 and p65 subunits in RAW 264.7 cells.^[23] Another Chinese medicinal formula, IBS-20, containing *C. chinensis* decreased LPS-stimulated pro-inflammatory cytokine secretion from JAWS II dendritic cells and also blocked the interferon gamma (IFN γ)-induced drop in transepithelial electric resistance which is an index of permeability, in fully differentiated Caco-2 monolayer.^[24] *C. chinensis* has also significant antimicrobial activity against a variety of microorganisms including bacteria, viruses, fungi, protozoans, helminths, and *Chlamydia*, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *E. coli*, *Propionibacterium acnes*, *Streptococcus pneumoniae*, *Vibrio cholerae*, *Bacillus anthracis*, *Bacillus dysenteriae*, and *Sa. cerevisiae*.^[7,21,25] Berberine, the major active component of *C. chinensis*, was found to be bactericidal on *V. cholera* and capable of inhibiting bacterial adherence to mucosal or epithelial surfaces.^[26]

Flos Lonicerae (金銀花 Jin Yín Huā)

Flos lonicerae is a honeysuckle flower belonging to Caprifoliaceae family. It is a widely used herb in China for the treatment of infection by exopathogenic wind-heat or epidemic febrile diseases.^[11,14,27,28] The dried flower and buds of *Flos Lonicerae* have shown various pharmacological effects including anti-nociceptive, anti-diabetic, anti-tumor, antioxidant, anti-angiogenic, antipyretic, antiviral, and hepatoprotective activities.^[6,29-31] *Flos Lonicerae* demonstrated anti-inflammatory properties through suppression of mediator release from the mast cells activated by secretagogues.^[32] In addition, the *n*-butanol fraction containing *Flos Lonicerae* can alleviate inflammation better than celecoxib

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