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Review

Naturally derived anti-inflammatory compounds from Chinese medicinal plants

Qiuhong Wang [a,b], Haixue Kuang [a,*], Yang Su [a], Yanping Sun [a], Jian Feng [a], Rui Guo [a], Kelvin Chan [c,d,**]

[a] Key Laboratory of Ministry of Education, Department of Pharmacology, Heilongjiang University of Chinese Medicine, Harbin, China
[b] The University of Sydney, NSW 2006, Australia
[c] Centre for Complementary Medicine Research, University of Western Sydney, NSW 2560, Australia
[d] Faculty of Pharmacy, The University of Sydney, NSW 2006, Australia

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ABSTRACT

Ethnopharmacological relevance: Though inflammatory response is beneficial to body damage repair, if it is out of control, it can produce adverse effects on the body. Although purely western anti-inflammatory drugs, orthodox medicines, can control inflammation occurrence and development, it is not enough. The clinical efficacy of anti-inflammation therapies is unsatisfactory, thus the search for new anti-inflammation continues. Chinese Material Medica (CMM) remains a promising source of new therapeutic agents. CMM and herbal formulae from Traditional Chinese Medicine (TCM), unorthodox medicines, play an improtant anti-inflammatory role in multi-targets, multi-levels, and multi-ways in treating inflammation diseases in a long history in China, based on their multi-active ingredient characteristics. Due to these reasons, recently, CMM has been commercialized as an anti-inflammation agent which has become increasingly popular in the world health drug markets. Major research contributions in ethnopharmacology have generated vast amount of data associated with CMM in anti-inflammtion aspect. Therefore, a systematic introduction of CMM anti-inflammatory research progress is of great importance and necessity.

Aim of the study: This paper strives to describe the progress of CMM in the treatment of inflammatory diseases from different aspects, and provide the essential theoretical support and scientific evidence for the further development and utilization of CMM resources as a potential anti-inflammation drug through a variety of databases.

Material and methods: Literature survey was performed via electronic search (SciFinder®, Pubmed®, Google Scholar and Web of Science) on papers and patents and by systematic research in ethnopharmacological literature at various university libraries.

Results: This review mainly introduced the current research on the anti-inflammatory active ingredient, anti-inflammatory effects of CMM, their mechanism, anti-inflammatory drug development of CMM, and toxicological information.

Conclusion: CMM is used clinically to treat inflammation symptoms in TCM, and its effect is mediated by multiple targets through multiple active ingredients. Although scholars around the world have made studies on the anti-inflammatory studies of CMM from different pathways and aspects and have made substantial progress, further studies are warranted to delineate the inflammation actions in more cogency models, establish the toxicological profiles and quality standards, assess the potentials of CMM

Abbreviations: Aβ, β-amyloid protein; AD, Alzheimer's disease; AP-1, Activator protein-1; AS, Atherosclerosis; CCl_4, Carbon tetrachloride; CFA, Complete Freund's Adjuvant; CIA, Type II collagen-induced arthritis; CMM, Chinese Material Medica; Con A, Concanavalin A; COX-2, Cyclooxygenase 2 protein; CP, Chinese Pharmacopoeia; DSS, Dextran sodium sulfate; HLJDD, Huang-Lian-Jie-Du decoction; ICAM-1, Intercellular adhesion molecule-1; IFN-γ, Interferon γ; IL, Interleukin; iNOS, inducible Nitric oxide synthase; LPS, Lipopolysaccharide; MCP-1, Monocyte chemoattractant protein-1; MDA, Malondialdehyde; MIA, Monosodium iodoacetate; MMP, Matrix metalloproteinase; MPTP, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; MyD88, Myeloid differentiation factor 88; NF-κβ, Nuclear factor-κβ; NO, Nitric oxide; NSAIDs, Non-steroidal anti-inflammatory drugs; 6-OHDA, 6-hydroxydopamine; OLE, Leaves of *Olea europaea* L.; OVA, Ovalbumin; p38 MAPK, Protein 38 mitogen-activated protein kinases; PD, Parkinson's disease; PGE 2, Prostaglandin E 2; PPARs, Peroxisome proliferator activated receptors; RA, Rheumatoid arthritis; Syk, Spleen tyrosine kinase; TAK1, TGF-β-activated kinase 1; TCM, Traditional Chinese Medicine; Th2, T helper-2; TLRs, Toll-like receptors; TNBS, Trinitrobenzene sulfonic acid; TNF-α, Tumor necrosis factor-α; UC, Ulcerative colitis; XXD, Xiexin decoction

* Correspondence to: Department of Pharmacology, Heilongjiang University of Chinese Medicine, No. 24 Heping Road, Harbin, China. Tel.: +86 451 82193001; fax: +86 451 82110803.
** Correspondence to: Building 5-Campbelltown, Locked Bag 1797, Penrith NSW 2751, Australia. Tel.: +61 2 4620 3837; fax: +61 2 4620 3291.
E-mail addresses: hxkuang@hotmail.com (H. Kuang), Kelvin.chan@sydney.edu.ac (K. Chan).

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in clinical applications, and make more convenient preparations easy to administrate for patients. Development of the clinically anti-inflammatory drugs are also warranted.

Contents

1. Introduction

Inflammation can be induced by many different stimulating factors, including physical damage, precursor chemicals, microbial invasion and immune responses (Kumar et al., 2003; Majno and Joris, 2004; Gregory and Barton, 2008). Generally speaking, controlled inflammation is a beneficial response that can defend and protect the body from harmful factors, but if the body's regulation of inflammation is dysfunctional, then inflammation will have an adverse effect on the body, such as the emergence of chronic inflammation and a series of chain reactions. A large number of inflammatory mediators lead to harmful effects on the body (Nathan, 2002, 2006; Medzhitov, 2008), including excessive degeneration, exudation, necrosis, or the formation of abnormal granulation formation, that result in different degrees of injury to the body (Serhan and John, 2005; Karin et al., 2006). Because inflammation involves many inflammatory mediators and pathways that lead to a wide range of changes in pathology, it is difficult to target the desired area when treating inflammation. The current treatment of inflammatory disorders in Western medicine often involves the extensive use of non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids. Recently, more attention has been focused on CMM (Chinese Material Medica) research and their anti-inflammatory efficacy, which results from their multi-component features including the ability to affect multiple targets and levels signaling pathways and their multiple mechanisms of mitigating inflammation (Drayton et al., 2006). Thus, the anti-inflammatory effects of CMM are receiving widespread attention, and a large number of mechanistic studies have been reported by experts worldwide showing the importance and necessity of researching CMM. However, there is no systematic review on the anti-inflammatory actions of CMM. Thus, the present review summarizes current research on the active ingredients, anti-inflammatory effects, and molecular mechanisms, as well as the development of drugs based on anti-inflammatory CMM with recommendations for future directions for the development and utilization of CMM.

2. Current treatment of inflammatory disorders using pharmaceutical drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) have been widely used to treat inflammatory disorders in clinical practice because of their fast onset of action and excellent curative effects. Side effects of NSAIDs include ulceration in the gastro-intestinal system (Gabriel et al., 1991; Allison et al., 1992; Hawkey, 2000), platelet dysfunction, and cerebral and cerebellar adverse effects (Aygün et al., 2012). Another popular category of anti-inflammatory drugs is the glucocorticoids, which have some adverse effects at high doses and with prolonged usage. Taken together, these two groups of pharmaceuticals are not ideal for treatment of inflammation. CMM, which have a long history in Chinese culture, can inhibit symptoms of several inflammatory diseases. Examples include Qi Jie Granule, which consists of the root of *Astragalus membranaceus* Bunge (黄芪), the resin of *Dranaena cochinchinensis* (Lour.) S.C. Chen (龙血竭), the root of *Angelica sinensis* (Oliv.) Diels (当归), the dried twig of *Cinnamomum cassia* Presl (桂枝) (Xu et al., 2007), the dried rattan of *Sargentodoxa cuneata* (Oliv.) Rehd. et wils. (大血藤), the root of *Rheum palmatum* L. (大黄), the resin of *Commiphora myrrha* Engl. (没药), the root of *Paeonia lactiflora* Pall. (赤芍), and the root of *Glycyrrhiza uralensis* Fisch (甘草), and has been found to have satisfactory curative effects when treating chronic pelvic inflammation through improving the blood viscosity and regulating T-lymphocytic subgroups (Zhang et al., 2004). Because some CMM have side effects, they must be subjected to specific treatments in order to reduce the toxicity of the crude drugs, namely processing of TCM, such as boiling, steaming, treating with salt or vinegar, frying, or charring, before they are used in decoctions or in the manufacture of herbal products (Zhao et al.,