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Review

Role of counter-current chromatography in the modernisation of Chinese herbal medicines

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ABSTRACT

This review focuses on the growing popularity of using counter-current chromatography (CCC), with its liquid stationary phase, as one of the prime methods for isolating compounds from Chinese herbal medicines (CHMs). 198 publications are reviewed covering 108 different plant species from 56 plant families. These describe the isolation of 354 different molecules across a wide range of polarities, chemical classes and molecular weights (in the range 100–1000 Da). The suitability of CCC for the separation of active compounds from CHM, the phase systems used, how CCC has developed in China, compounds isolated, CCC instrumentation, performance, operational issues and innovations, all supported by detailed cross-referencing, are described. It is concluded that CCC is making an increasingly important contribution to the modernisation of Chinese herbal medicines.

Contents

1. Introduction

The signing of the Beijing Declaration on the modernisation and internationalization of Chinese medicines on 29 November 2007 at the Conference on the International Science and Technology Cooperation in Traditional Chinese Medicine in Beijing, was the catalyst for this review of the role counter-current chromatography (CCC) is playing and has played in the modernisation process. The declaration states that:

> "*the combination of traditional Chinese medicine and other schools of medicine may lead to a novel healthcare model for humans, and will effectively lower healthcare costs for both individuals and institutions. Innovation and diffusion of traditional Chinese medicine needs the support of modern science. Newly emerged disciplines, such as genomics, and the steady growth of basic knowledge, in*

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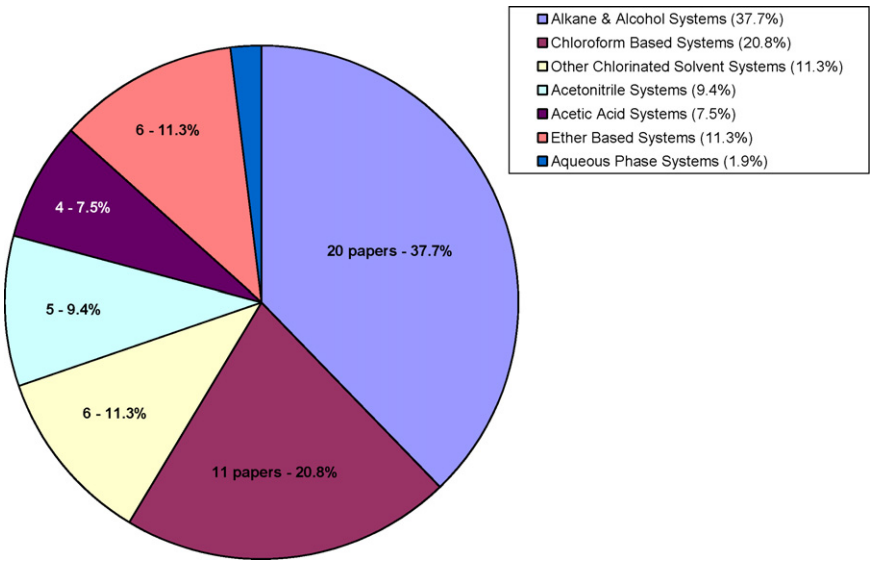

Fig. 1. Pie chart showing the families of phase systems used in the 198 paper reviewed.

particular, bioinformatics, has provided both the means and way forward for interpreting the basic principles of traditional Chinese medicine, and is leading to associated innovation. It is necessary to promote innovations of traditional Chinese medicine through enhanced international cooperation, in an attempt to further enrich its theoretical knowledgebase, improve people's understanding of traditional Chinese medicine, raise the level of safety, effectiveness, and quality of traditional Chinese medicine, and accelerate the modernization and internationalization of the traditional Chinese medicine industry."

The 198 papers reviewed [1–198] cover 354 different molecules from 108 different plant species and involve research collaborations across 109 different organizations. Details of the range of plant species/families studied, the compounds isolated and their numerous medical indications are given. Author, organizational and operational details are contained in a supplement to this review.

2. The growth of interest in Chinese herbal medicines

Since the 1968 Medical Act which deregulated medical practice and allowed Chinese and other herbal practitioners of all kinds to practice without a licence in the UK, the British market for Chinese herbal remedies has been growing at about 20% per annum and there are now well over 1000 registered practitioners in the UK [199]. However, there have been increasing concerns about the safety issues surrounding the unregulated use of traditional Chinese medicine (TCM) approaches, particularly after the mistaken use of a toxic Aristolochia species by a slimming clinic in Belgium resulting in more than 100 cases of renal failure of which some were fatal [200]. The EU Directive on Traditional Herbal Medicinal Products (agreed in April 2004) came into force on 30th October 2005. There will be a transitional period for products legally on the market on 30 April 2004, giving them protection until 2011. The Directive requires traditional, over-the-counter herbal remedies to be made to assured standards of safety and quality and for regulations to be standardised across Europe [201]. This new legislation is making manufacturers simplify, modernise and upgrade their products sometimes using the western reductionist approach and sometimes developing new approaches, which are an interesting synthesis of both Eastern and Western culture. For example Professor Guoan Luo of Tsinghua University, Beijing is using a new "omics" approach, chemomics, where "the phytochemical composition of a herbal formula with demonstrated clinical efficacy is regarded as a global chemome, which can be simplified successively through bioactivity-guided screening to achieve an optimized chemomome with minimal phytochemical composition for further drug development", while maintaining its curative effect for a specific disease [202]. Professor Luo calls this a "modernized composite medicine" or MCM.

3. Counter-current chromatography

Counter-current chromatography is a liquid–liquid partition chromatography process where both the mobile and stationary phases are liquids [203]. The "column" is simply a long length of tubing wound on a drum (the bobbin) which is geared to the main rotor in such a way that it simultaneously rotates at twice the speed of the rotor (planetary motion). This double motion sets up a fluctuating force field which forces one phase (the less dense or lighter

Table 1
A list of phase system families with an analysis of their usage in publications over time.

Phase system family	1988–1999	2000–2003	2004	2005	2006	2007
Alkane and alcohol systems (37.7%)	7	20	16	39	33	33
Chloroform-based systems (20.8%)	14	14	2	6	2	6
Other chlorinated solvent systems (11.3%)	0	0	6	1	1	1
Acetonitrile systems (9.4%)	0	0	0	1	3	3
Acetic acid systems (7.5%)	0	0	1	1	1	3
Ether-based systems (11.3%)	2	3	1	4	0	1
Aqueous phase systems (1.9%)	1	1	0	0	0	0
Total	24	38	26	52	40	47