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Short communication

A pilot study of direct infusion analysis by FT-ICR MS for rapid differentiation and authentication of traditional Chinese herbal medicines

Fei Han, Yanting Li, Xiaoshu Zhang, Aihua Song, Heyun Zhu, Ran Yin *

School of Pharmacy, Shenyang Pharmaceutical University, Shenyang 110016, China

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ABSTRACT

The feasibility of direct infusion analysis in a Fourier-transform ion cyclotron resonance mass spectrometer (FT-ICR MS) for fast differentiation and authentication of traditional Chinese herbal medicines (TCHMs) was evaluated for the first time. The widely used Gardenia jasminoides Ellis and the clinical preparations Kudiezi injection were selected as model samples and analyzed by this method. With minimal or no sample pretreatment, 30 and 29 peaks which were corresponding to 43 and 40 chemical constituent respectively were rapidly detected and tentatively identified according to the accurate mass information and MS/MS data within only few minutes, including iridoids, phenolic acids, glucosides, flavonoids, nucleosides and sesquiterpene lactones. Our results demonstrated that direct infusion analysis in FT-ICR MS could provide a rapid, solvent saving and environmental friendly method for the differentiation and authentication of TCHMs, and it may be applicable to other plants.

1. Introduction

Traditional Chinese herbal medicines (TCHMs) are becoming increasingly popular worldwide, mainly because of their high efficacy, low cost, ease of access, and few adverse effects [1–3]. It is widely accepted that the effects of TCHMs are brought about by their chemical constituents. However, the chemical composition and quality of TCHMs may vary greatly because of the genotype, growing environment, and interactions between genotype and environment. Thus, the rapid chemical constituent differentiation and authentication for TCHMs is significative because it can help us to timely and clearly understand if there is any different chemical composition among these TCHMs and how different they might be [4,5].

Up to now, fingerprinting techniques such as liquid chromatography coupled to mass spectrometry (LC–MS) and chromatographic fingerprints have been utilized in differentiating TCHMs with different genotypes, from different growing environment, or from different plant parts [6–9]. However, sample pretreatment and chromatographic separation are always required before MS analysis. And the technique can be both time and solvent consuming even if UPLC–MS was utilized [3]. Thus, there is still a demand to develop simple and solvent-saving methods for rapid differentiation and authentication of TCHMs and their preparations.

Fourier transform-ion cyclotron resonance mass spectrometry (FT-ICR MS) is well known because of its ability to achieve an ultra-high resolving power by accumulating time-domain transient signals in different time-domain data sets ($m/\Delta m50\%$ 200,000, in which $\Delta m50\%$ is the full peak width at half-maximum peak height of $m/z = 400$) with high mass accuracy [10]. FT-ICR MS can be a viable method to directly analyze chemical structures of each constituent molecule in a very complex mixture by increasing resolving power and accurate mass measurement without the need for any prior extraction or separation steps. Several research groups have recently applied this method to study many complex organic mixtures such as oil, coconut juice and metabolic samples [11–16]. However, few studies to date have described its use in studying the chemical composition of TCHMs.

In the present study, the feasibility of direct infusion analysis for fast differentiation and authentication of various components from TCHMs based on FT-ICR MS was evaluated. The widely used TCHMs Gardenia jasminoides Ellis and the clinical preparations Kudiezi injection were selected and analyzed as model chemical component system based on previous research [17–21]. Only 2 min were required for the study of each sample, including sample introduction and MS analysis time. The reliability of this method was tentatively assured by the accurate m/z values and MS/MS data obtained from TCHMs samples. To the best of our

* Corresponding author. Tel.: +86 02423986263.
E-mail address: yinran_syspu@163.com (R. Yin).

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knowledge, this is the first report on the application of FT-ICR MS to study TCHMs by direct infusion analysis. Thus, direct infusion analysis in FT-ICR MS could be an optional and useful tool for rapid differentiation and authentication of other TCHMs and their preparations.

2. Material and method

2.1. Samples and reagents

Gardenia jasminoides Ellis was purchased from Tianyitang Drug store (Shenyang, China) and identified by Associate Professor Yuan Jiuzhi (Department of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University). Ku-die-zi injection was obtained from Tong Hua Huaxia Pharmaceutical Co., Ltd. (Tonghua, China, No.: 140110). Methanol and formic acid of HPLC grade were purchased from Fisher Scientific (Fair Lawn, NJ, USA) and Sigma–Aldrich (Steinheim, Germany), respectively. Other reagents were of analytical grade. Ultrapure water was filtered through a Milli-Q system (Millipore, Milford, MA, USA).

2.2. ESI FT-ICR MS conditions

Prior to the first analysis, sodium formate solution was used to calibrate FT-ICR MS equipped with a 7.0 T superconducting magnet (Bruker Daltonics, Bremen, Germany). Briefly, the sample was directly infused at a flow rate of 120 μL/h into the ESI source. The mass spectrometer was set to operate over a mass range of m/z 150–1000 in the negative ion mode analysis owing to the high signal response. The ESI source conditions were as follows: a nebulizer gas pressure of 1.2 bar, a dry gas flow rate of 4.0 L/min, a capillary voltage of −3.5 kV, an ion flight time of 0.8 s, an ion accumulation time of 0.2 s and a transfer capillary temperature of 200 °C. Each spectrum was acquired by accumulating 50 scans of time-domain transient signals in 8 mega-point time-domain data sets. A resolving power $m/\Delta m50\% = 280{,}000$ and a mass accuracy of <3 ppm provided the unambiguous molecular formula assignments for singly charged molecular ions. In the MS/MS experiments, collision-induced dissociation (CID) mode was selected, argon was used as the collision gas, the collision energy was adjustable from 6 eV to 25 eV, the isolation windows were set as 10 m/z and collision RF amplitude was set as 1200 Vpp. FT-MS control software was used to control the equipment. The mass spectra were acquired and processed using Data Analysis software (Bruker Daltonics, Bremen, Germany). The MS data were processed and the elemental compositions of the compounds were determined by measuring the m/z values. To avoid the cross-contamination, a blank run was inserted between sample runs.

2.3. Preparation of samples

Firstly, the dry herbal medicine powder of Gardenia jasminoides Ellis (0.5 g) was accurately weighed and ultrasonic-extracted with 25 mL 100% methanol for 30 min. And then the solution was centrifuged at 10,000 rpm for 2 min. An aliquot of the supernate was filtered through a 0.22 μm membrane before injection.

And then, Kudiezi injections were stored at 4 °C prior to analysis. All samples were centrifuged at 15,000 rpm for 3 min. An aliquot of the supernate was filtered through a 0.22 μm membrane before analysis. Meanwhile, to choose the most appropriate dilution, the supernate with different dilutions by 0.1% formic acid (2-fold, 5-fold, and 10-fold) was infused into the mass spectrometer for a pilot study for both methods. 5-fold dilution was ultimately selected because maximum number of peaks (S/N > 5) were detected and most of the ions showed the best overall response.

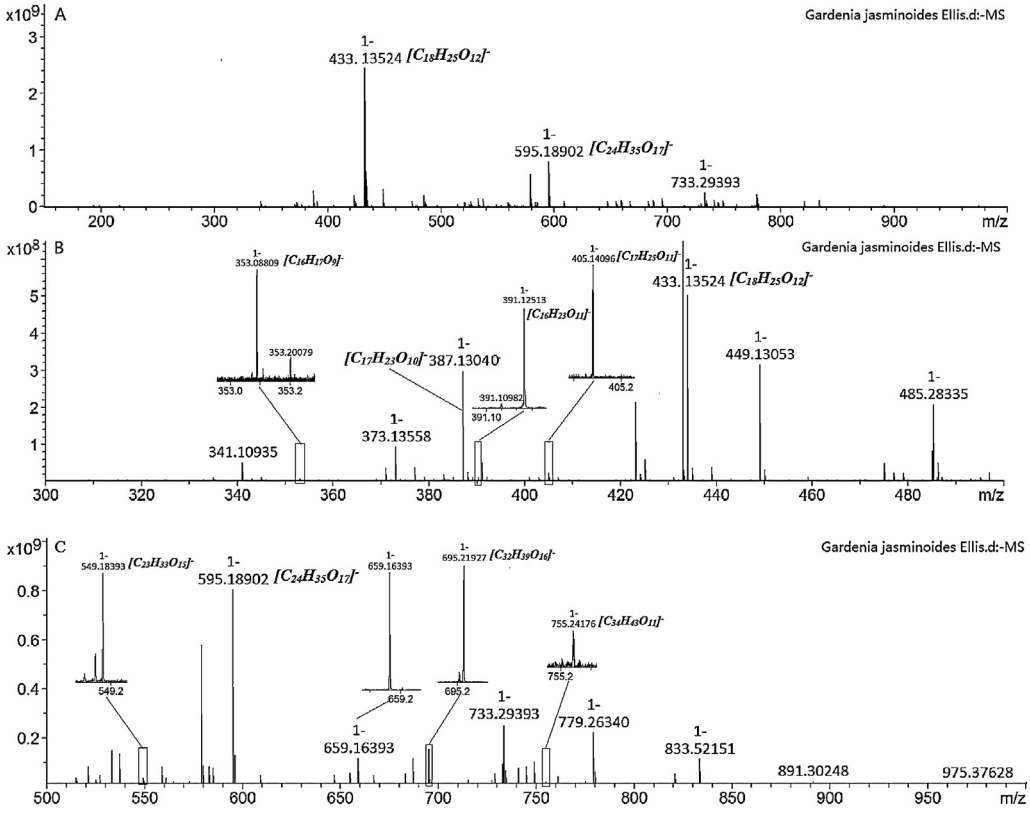

Fig. 1. The FT-ICR MS spectra of *Gardenia jasminoides Ellis extract* after direct injection analysis. A: m/z range 150–1000; B: 300–500; C: m/z range 500–1000.