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Effects of ion source operating parameters on direct analysis in real time of 18 active components from traditional Chinese medicine

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ABSTRACT

Direct analysis in real time mass spectrometry (DART-MS) provides a new analytical method for traditional Chinese medicine (TCM). The present study investigated the effects of key ion source operating parameters on DART-MS analysis of various TCM active components. A total of 18 active components, including phenylpropanoids, alkaloids, saponins, flavones, volatile oils, and glycosides, were examined. For each substance, the peak area and signal-to-noise of its characteristic ions under different reagent gases and heater temperatures were compared. Based on the comparison, the relationships among chemical structures, ion source parameters and instrument responses were revealed. Finally, some suggestions about choosing reagent gas and heater temperature were proposed for types of TCM active substance, which offered a reference for the application of DART-MS on TCM analysis.

1. Introduction

Direct analysis in real time (DART) is an open air desorption ionization source first introduced in 2005. It demands no or little sample pretreatment and allows direct and fast detection [1]. It is believed that the mass spectrometric analysis of complex sample would be greatly shortened by this novel technique [2]. Benefiting from the above advantages, DART has presented great potentials in the field of chemical and biochemical analysis, such as screening of counterfeit drug, food safety, forensic expertise and clinical examination [3–5]. Coupling with types of mass spectrometry (MS), DART has been drawing attention in the quality control of traditional Chinese medicine (TCM), particularly in the application area of authentication [6,7]. In recent publications, the use of DART-MS has expanded to TCM in various form, including decoction pieces and preparations [8,9].

In DART-MS experiments, it is the same case with other analytical tools that choosing proper operational conditions is important. Several parameters have been reported to affect the DART-MS experimental results. Three kinds of insert gas, i.e., helium (He), argon (Ar) [10], and nitrogen (N_2) have been employed as the reagent gas of DART-MS analysis [11]. The ionization energy of these three gases is 19.8 eV, 11.5 eV, and 8.5–15.5 eV, respectively [12]. With the highest energy, high-purity He is the most frequently used but also the most expensive one. It is well known that TCM comes from natural sources and consists of numerous substances with various physical and chemical properties. The character of TCM provides the possibility of choosing the type of reagent gas according to different TCM samples. For the reason of economy, substituting He with Ar or N_2 in some cases will promote the application of this technique.

On the other hand, through heating the reagent gas, the DART heater can influence the thermal-desorption and ionization process of target substances [11,13]. Several studies have shown that the improvement of sensitivity could be achieved by the increase of heater temperature [14]. However, it is worth noting that some TCM may contain thermal-sensitive components, and too high temperature would induce the decomposition of these compounds [1]. In conclusion, the reagent gas and heater temperature are the key factors affecting DART-MS analysis, and the two parameters should be carefully optimized for different samples.

In this work, eighteen compounds from phenylpropanoids, alkaloids, saponins, flavones, volatile oils, and glycosides were chosen as common TCM active substances. For the purpose of providing the basis for choosing the reagent gas and heater temperature, the effects of aforementioned DART operating parameters on the analytical performance of these components were investigated.

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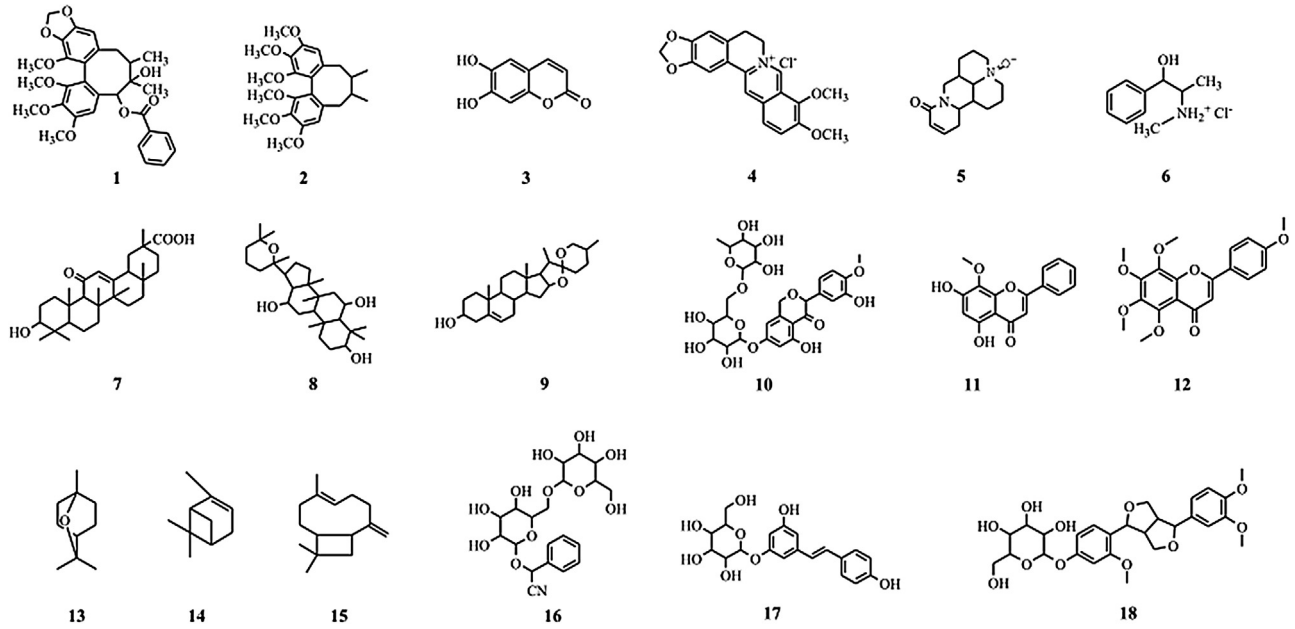

Fig. 1. Chemical structures of the used standards: 1. schisantherin A; 2. deoxyschizandrin; 3. aesculetin; 4. berberine hydrochloride; 5. oxysophocarpine; 6. ephedrine hydrochloride; 7. glycyrrhetintic acid; 8. panaxatriol; 9. diosgenin; 10. hesperidin; 11. wogonin; 12. tangeretin; 13. eucalyptol; 14. α-pinene; 15. *trans*-caryophyllene; 16. amygdaline; 17. polydatin; 18. forsythin.

2. Materials and methods

2.1. Reagents

HPLC-grade methanol was supplied by Merck (Darmstadt, Germany). Ultrapure water was produced in the laboratory with the Milli-Q water purification system (Molsheim, France). Standard substances including schisantherin A, deoxyschizandrin, berberine hydrochloride, oxysophocarpine, ephedrine hydrochloride, glycyrrhetintic acid, panaxatriol, diosgenin, wogonin, amygdaline, and forsythin were received from the National Institutes for the Control of Pharmaceutical and Biological Products (Beijing, China). Aesculetin, hesperidin, tangeretin, and polydatin were provided by Shanghai Winherb Medical Technology Co., Ltd. (Shanghai, China). Eucalyptol, α-pinene, and *trans*-caryophyllene were purchased from Sigma–Aldrich (St. Louis, MI, USA). Fig. 1 shows the chemical structure of the eighteen standards.

All the standard substances, except for eucalyptol, α-pinene, and *trans*-caryophyllene, were dissolved with 50% methanol–water (v/v, 0.5 mol/L). Three volatile oils were directly analyzed without any pretreatment. All the samples were stored at 4 °C prior to analysis. Sample analysis was conducted with three replicates, and their averages were recorded.

2.2. DART-MS equipment and ionization conditions

DART-MS analysis was carried out using a DART-SVP ionization source (IonSense, Saugus, MA, USA) interfaced to a triple-quadrupole mass spectrometer (MDS SCIEX API4000, Applied Biosystems, Foster City, CA, USA). High-purity helium (He), high-purity nitrogen (N_2), and high-purity argon (Ar) were selected as the ionizing mediums, respectively. During the sample analysis, the ionizing mediums was heated and transferred under the pressure of 0.17 MPa, to form a hot gas stream for thermo-desorption and ionization of analytes. Sample coated glass tubes were placed on the dip-it sampler, and passed through the gas beam at a speed of 0.2 mm s^{-1}. The sample was positioned away from the DART outlet with a distance of 10 mm. MS was adjusted to the positive or negative ion mode with selected ion monitoring (SIM). DART was also operated either in a positive ion mode or a negative ion mode. The grid electrode at the DART exit gun and the entrance potential (EP) on mass spectrometer were ±450 and ±10 V, respectively. Declustering potential (DP) of each compound is shown in Table 1. All the operations of DART and MS were controlled by DART v.3.0.3b and Analyst 1.5.0 software, respectively.

3. Result and discussion

3.1. DART-MS analysis of phenylpropanoids

Schisantherin A, deoxyschizandrin, and aesculetin are phenylpropanoids, where achisantherin A and deoxyschizandrin are lignans, while aesculetin is coumarins.

Fig. 2a and b exhibits the characteristic ion signals of schisantherin A in DART-MS ion chromatogram under different reagent gases and heater temperatures. As shown in Fig. 2a, the order of magnitude of the ion peak area under He is 1–2 higher than that under Ar and N_2. However, the intensities of instrument noise under the three reagent gases are He > N_2 > Ar. The signal-to-noise ratio (*S*/*N*) is varied differently from the peak area of the ion signals. It could be observed in Fig. 2b that, as the heater temperature increases from 200 to 500 °C, the *S*/*N* of ion signal increases rapidly. Interestingly, when the heater temperature exceeds 400 °C, the characteristic ions of schisantherin A exhibits similar *S*/*N* under He and Ar. Therefore, during the DART-MS analysis of schisantherin A, Ar has the potential to be an alternative to He with the heater temperature over 400 °C, and N_2 could be employed as reagent gas with heater temperature of 500 °C.

Fig. 2c and d displays the characteristic ion signals of deoxyschizandrin in DART-MS ion chromatogram under different reagent gases and heater temperatures. Compared with schisantherin A, deoxyschizandrin has lower boiling point and is easier to thermo-desorbed from analyte. Hence, deoxyschizandrin could be analyzed by DART-MS with a relatively lower temperature. Unfortunately, when the heater temperature is over 300 °C with He or 400 °C with N_2, the peak area and *S*/*N* of the characteristic ions