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High throughput molecular weight confirmation of Pharmaceutical Compounds using DART MS analysis with ultra-fast polarity switching

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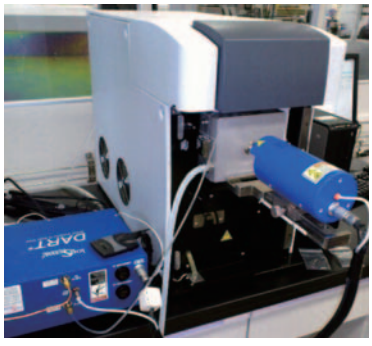
Introduction

DART, a direct atmospheric pressure ionization source, is known to have little or no negative effect from the solvent used to dissolve the sample. Even with problematic solvents for LC/MS operation such as non-volatile solvents or solvents containing salt, the target compounds can be instantly identified using DART-MS without any sample preparation. High-throughput molecular-weight (MW) confirmation of synthesized compounds is difficult to achieve using time of flight mass spectrometers, which have been a common choice to interface DART, due to its limitation in switching between positive and negative ion modes. By combining an automated DART ion source with a quadrupole mass spectrometer with ultra-fast polarity switching capability, 11different pharmaceutical compounds with various polarities were successfully determined in approximately 10 sec/sample.

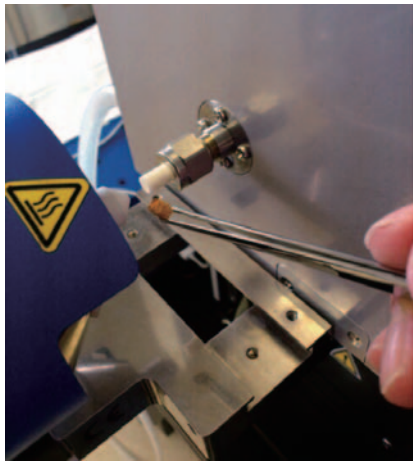
Materials and Methods

DART-MS analyses of 10ppm pharmaceutical compounds dissolved in 100% DMSO were carried out. The DART-SVP ion source (IonSense Inc., MA, USA) was coupled to the single quadrupole LCMS-2020 (Shimadzu Corporation, Kyoto, Japan), and DART-ID CUBE (IonSense), the new type of DART, was also coupled to the said mass spectrometer. Introduction of samples for DART-SVP was automated by using the X-Z scanner, which is capable of automating up to 96 samples/run. Ultra-fast polarity switching was utilized on the mass spectrometer to collect full scan data. LCMS-2020 can achieve the polarity switching time of 15msec and the scanning speed of up to 15000u/sec, therefore the loop time can be set at less than 1 second despite the relatively large scanning range of 100-1000 u.

(a)



(b)



(c)

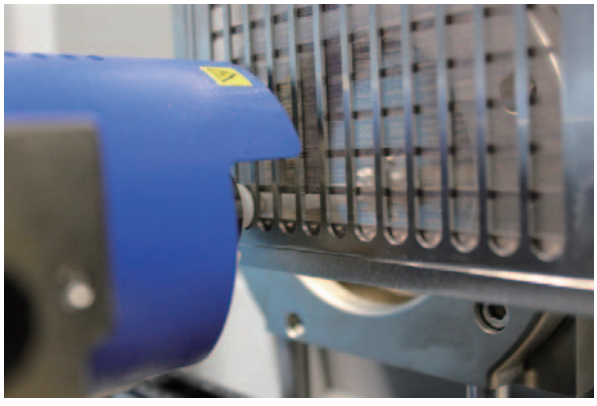


Fig. 1 DART-SVP ion source & LCMS-2020
(a) DART-SVP & LCMS-2020 Overview; (b) DART-SVP interface enlarged view;
(c) DART-SVP interface using the X-Z scanner

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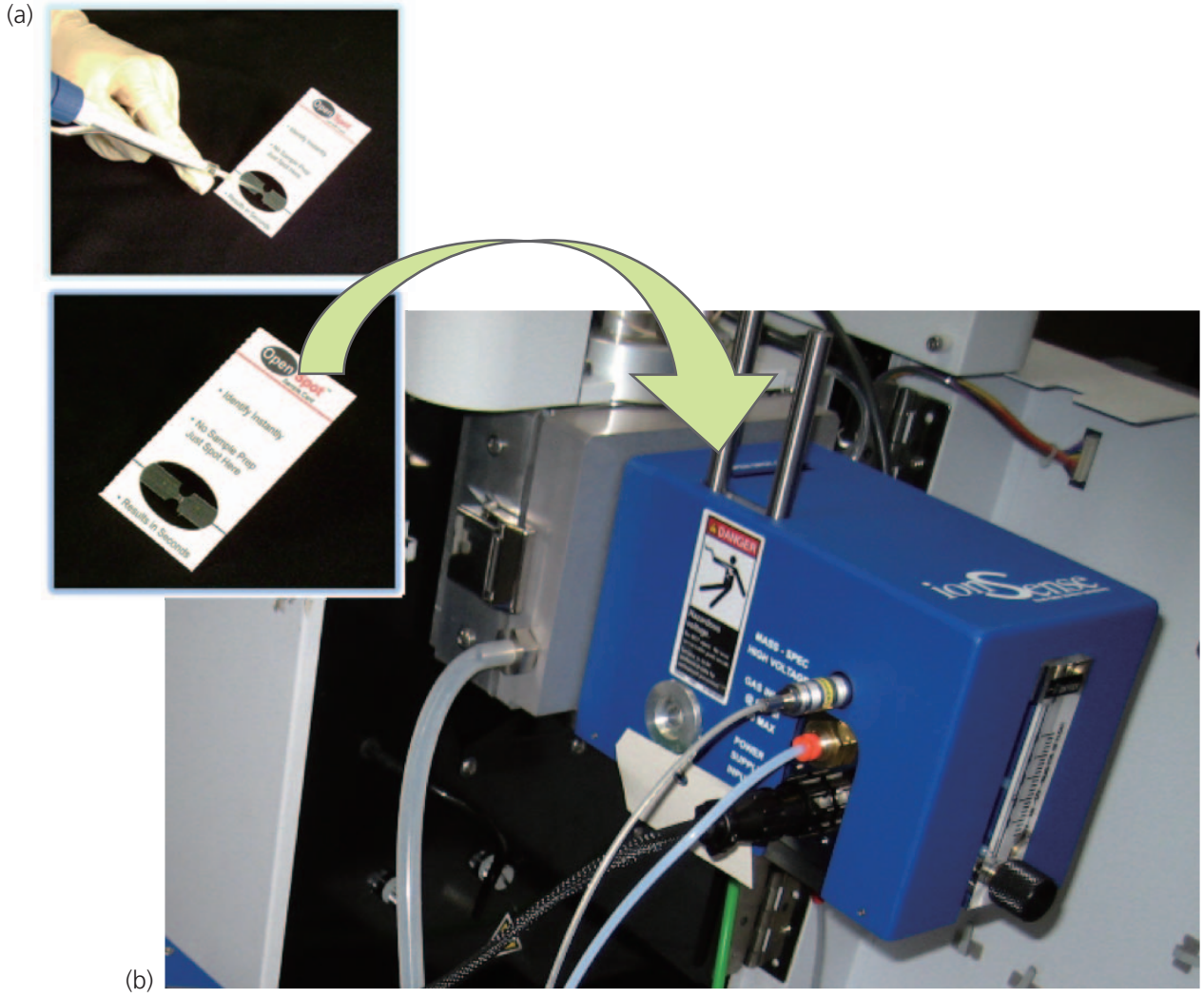

Fig. 2 DART-ID CUBE ion source & LCMS-2020
(a) The OpenSpot Sample Card; Spot solution with pipettor, or place droplet of liquid containing analyte on center spot, then card is ready to analyze
(b) DART-ID CUBE & LCMS-2020 Overview; arrow shows the guide slot which the sample card is inserted into.

Results

DART-ID CUBE

First, the new DART-ID CUBE ion source was tested and successfully interfaced to LCMS-2020. As ID CUBE required external high voltage (HV) from LC/MS instruments, HV supply of LCMS-2020 easily connected to ID CUBE. Mass spectrum was identified for both the positive standard sample of 100 ppm quinine and the negative standard sample of 100 ppm methylparaben. 5 uL of samples were spotted on a specialized sampling card and inserted into the ID CUBE source. Vaporization of sample is more rapid with ID CUBE than it is with DART-SVP since the sample is directly heated with electric current running through the metal mesh on which the sample is applied, while the DART-SVP heats the sample with heated gas.

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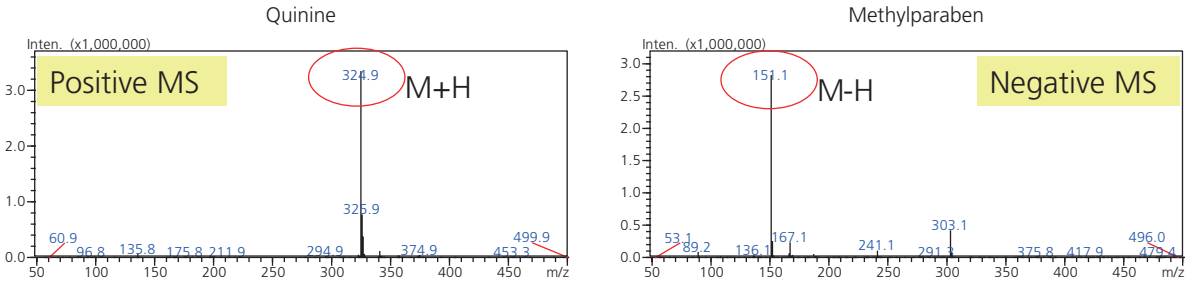

Fig. 3 Standard sample MS spectra using DART-ID CUBE

DART-SVP

Next, the DART gas (helium) heater temperature was raised to 350°C and commercially available pharmaceutical compounds such as Atenolol, Warfarin, Yohimbine, Cilostazol, Nifedipine, Diazepam, Nitrendipine, and Diphenhydramine were applied on a metal mesh of the X-Z tool, which has the same size and configuration as the 96 well microtiter plate, to automatically introduce them into the DART ionization gas.

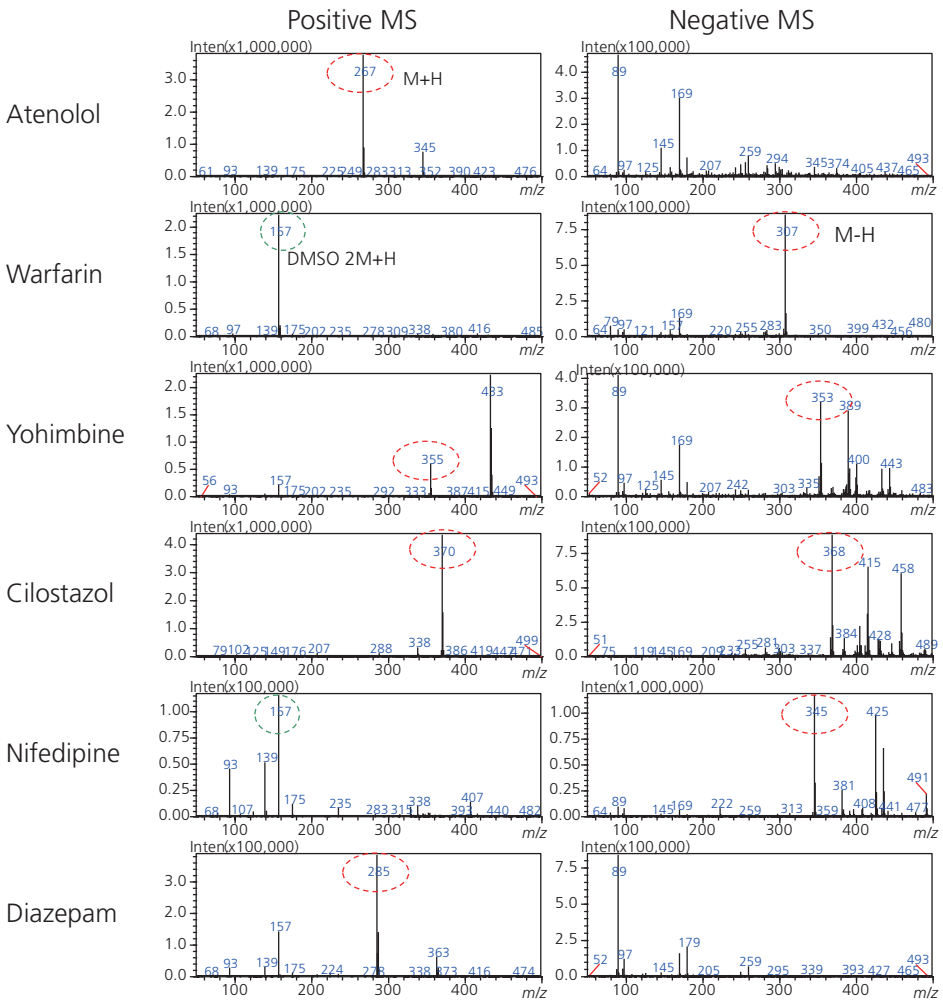

Fig. 4a Pharmaceutical compounds DART-MS analysis results

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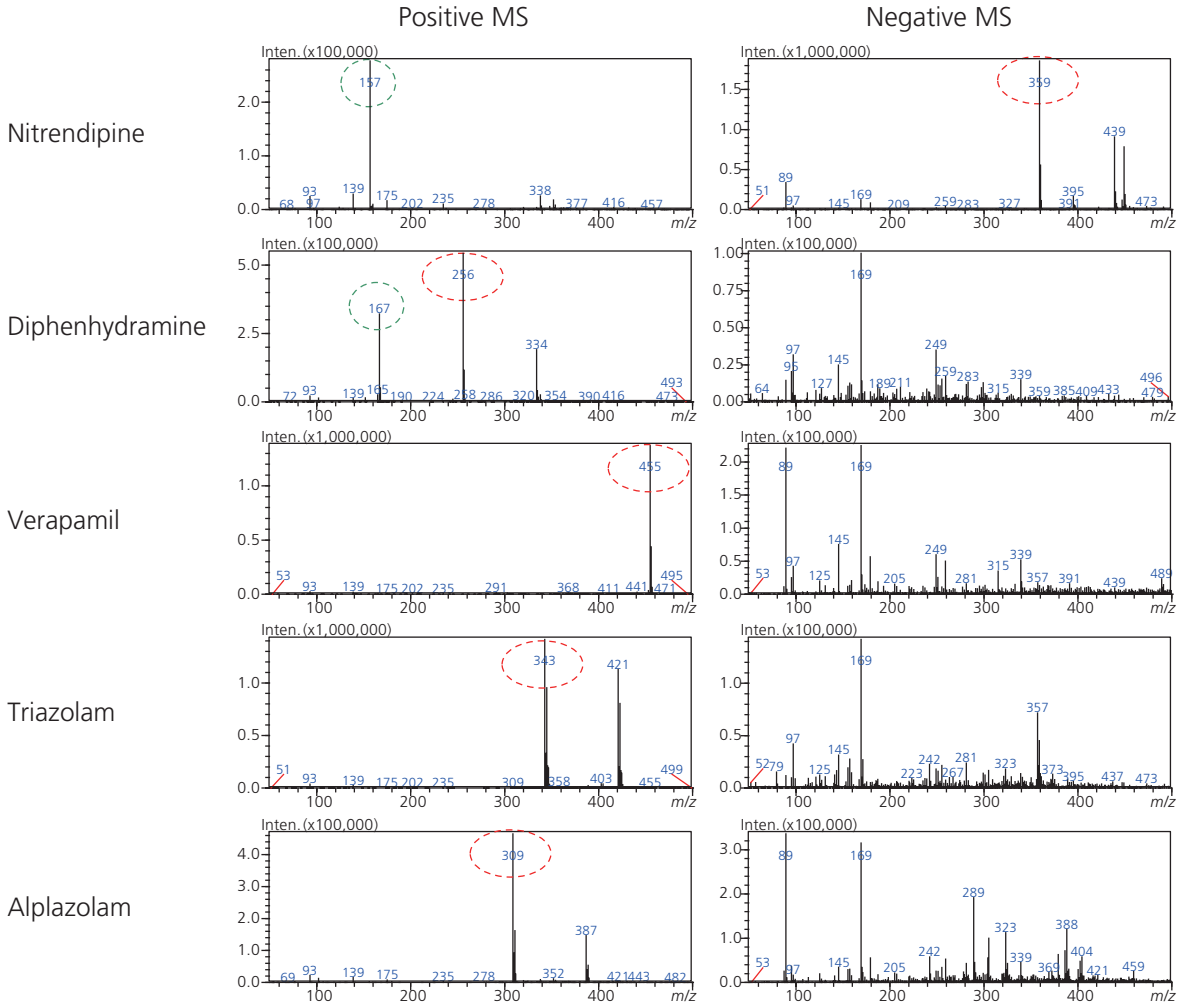

Fig. 4b Pharmaceutical compounds DART-MS analysis results

Relatively large DMSO peak was observed in positive mode scan, but the target compounds were successfully identified as well. Positive ion spectrum was observed for Atenolol, Diazepam, Diphenhydramine, Verapamil, Triazolam and Alplazolam. Negative ion spectrum was observed for Warfarin, Nifedipine and Nitrendipine. Both positive and negative ion spectra were observed for Yohimbine and Cilostazol. DART-MS with the ultra-fast polarity switching and ultra-fast scanning demonstrated its ability to perform high throughput analysis of pharmaceutical compounds dissolved in DMSO as solvent at analysis speed @ approximately 10 sec/sample.

Conclusions

- 11 different pharmaceutical compounds were analyzed by DART & LCMS-2020.
- With DART, the choice of solvent for the preparation of sample rarely poses a problem. Here the samples were dissolved in concentrated DMSO.
- The capability of LCMS-2020 to do ultra high-speed polarity switching was fully utilized.
- Target ions were detected in positive and/or negative mode for all samples.

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