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A novel data processing algorithm “Mass-it” that generates MS-labeled UV chromatograms for facilitating impurity analysis using single quadrupole LC-MS

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1. Introduction

- In pharmaceutical and chemical industry, chemists use HPLC and LC-MS to qualify and quantify components in synthetic products, many of which are analyzed using only the UV detector of LC.
- The advantages of LC-MS include sensitivity and qualitative performance. However, the complexity of data analysis, low robustness, and limitation of target compounds by ionization method have hindered the introduction of LC-MS.
- To increase implementation of LC-MS for impurity analysis, we designed the instrument that helps the transition process in three respects: 1) assisting overall interpretation of MS data by a novel deconvolution algorithm named “Mass-it”, 2) demonstrating the contaminant-proof robustness of the instrument, and 3) providing the ion source that serves for a wide range of applications.

2. Methods

Chemical standards (atorvastatin, propranolol, simetryn, quintozene) were purchased from FUJIFILM Wako Pure Chemical (Japan). Analysis was performed using the Nexera XR system consisting of LC-40B XR pumps, SIL-40C XR autosampler, CTO-40C column oven, and SPD-M40 photodiode array detector and the LCMS-2050 compact-sized single quadrupole mass spectrometer (Fig. 1).

Atorvastatin were analyzed by the scan mode (*m/z* 100-1000) using ESI/APCI dual ionization source (Dual Ionization Source: DUIS) and in positive and negative modes. Default MS parameter of LCMS-2050 were used such as gas flow rate and desolvation temperature.

Fig. 1 Shimadzu LCMS-2050 integrated into Nexera series UHPLC.

3. Results

- **Mass-it** processes the TIC chromatogram peaks and generates a list of detected mass signals with retention times determined via the extracted ion chromatograms. The XIC retention times enable the algorithm to distinguish between multiple co-eluting component signals and a group of related ion signals derived from a single component. Background signals are also eliminated as they do not exhibit a peak-top needed for determining the retention time.
- The *m/z* of listed components by Mass-it are labeled onto the UV chromatogram. The example shown in **Fig. 2** is a representative data for a high-purity sample, detecting only a single component throughout. Because the algorithm is known to label multiple components if detected, the data simply summarizes that only a single component was detected from this sample. The application of Mass-it for impurity detection was also demonstrated (**Fig. 3**).

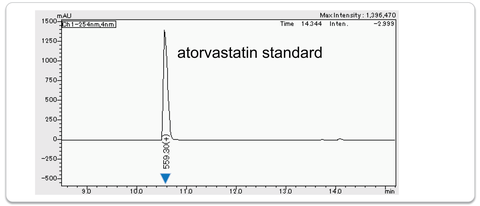

Fig. 2 UV chromatogram of atorvastatin with apparently a single component, and Mass-it labeling the peak correctly with a single *m/z*.

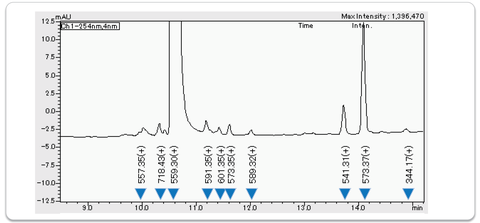

Fig. 3 Atorvastatin impurities labeled with *m/z* generated by Mass-it.

- We performed the **accelerated aging test** by introducing 30 mg of compounds in 10,000 consecutive injections (a standard mixture of three pharmaceutical compounds at 1000 ng/μL each was injected 1 μL at a time). Performance of the LC-MS was checked at intervals during this experiment in the MS scan mode. We observed 8.5% RSD for the peak areas analyzed and no decrease in the area value (**Fig. 4**). The results suggested that stable results can be obtained even if high-concentration samples such as synthetic products are repeatedly analyzed.

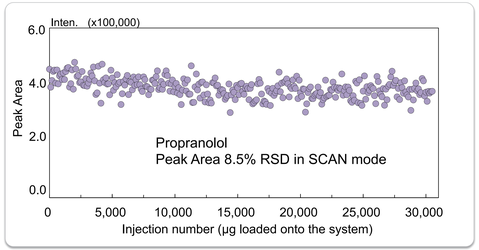

Fig. 4 Long-term stability study on LCMS-2050 showing resistance to high sample loads.

- This contaminant-proof robustness may be attributed to three technologies implemented in the LC-MS hardware:
  - ✓ Large diameter of the ion inlet preventing it from clogging.
  - ✓ Heated ESI gas spraying off-axis towards the upper side of the ion inlet, which is designed to prevent contaminants from entering into the MS vacuum.
  - ✓ Mitigating the charge-up of quadrupole rods and lens component surface by applying a sweeping voltage in between acquisitions. This ensures efficient ion transmission even when contaminant accumulation is inevitable.

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- The LCMS-2050 is equipped with the **DUIS ionization unit** that generates ions by both ESI and APCI pathways. The ionization capability of the DUIS interface was evaluated using compounds that are characteristically ionized by ESI and APCI (**Fig. 5**).
- The ionization efficiency of simetryn by DUIS was comparable to ESI-only configuration, showing that the addition of APCI capability has only marginally compromised the ESI capability in the DUIS configuration. Thus, it is a versatile and universal ion source that can be used for a wide range of compounds in a single analysis.

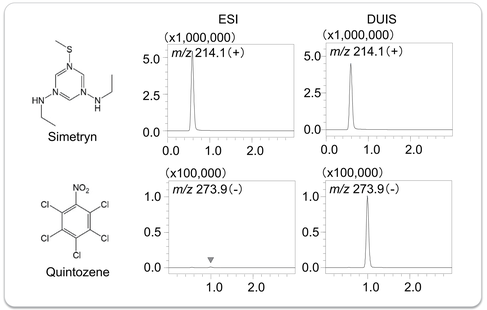

Fig. 5 Mass chromatograms of simetryn (top) and quintozene (bottom) measured with the DUIS to enhance APCI.

4. Conclusion

- ✓ The LCMS-2050 is extremely robust and equipped with software features to make LC-MS data more comprehendible even to first-time LC-MS users. These features are hoped to increase more LC-MS usage for impurity analysis.

Reference

- K Koterasawa et al., “Technical background for the LCMS-2050, a compact mass detector for LC” , Shimadzu Corp. technical report, C146-E453, 2022
- K Koterasawa et al., “ Improvement of liquid chromatograph performance by Mass-it™ function”, Shimadzu Corp. technical report, C146-E454, 2022