Developing Direct Analysis in Real Time Mass Spectral Libraries for the General Unknown Screening of Drugs

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Overview

- A drug of abuse DART-MS database has been created using in-source CID data acquired from a single quadrupole MS for targeted drug screening.
- A software program was developed in-house to search the library and match unknown spectra against the DART database with a reverse library search approach.
- Current database contains 700 drug-related substances, including opioids, cannabinoids, cathinones, benzodiazepenes, and various designer drugs.

Introduction

- There is an ever increasing need for rapid and more specific drug screens to combat current and emerging drug abuse trends.
- In the past, synthetic cathinones and cannabinoids were heavily prevalent in the United States. The trend has since drastically shifted towards opioid abuse.
- Drug abuse trends are constantly shifting, creating difficulties and challenges for their detection.
- Here a DART-MS drug library has been created using a software program developed in-house. The data was acquired using a mobile single quadrupole mass spectrometry platform. This database can be used for the general unknown screening of a wide range of drug compounds.

Methods

- Drug standards were all provided by Cayman Chemical.
- A thermal profile mass analysis was performed for each standard using temperatures from 150°C to 450°C in increments of 100°C.
- Cone voltage varied between **15, 30, 50, and 70 V** for each MS acquisition.
- DART-MS spectra at the optimal DART temperature for each drug compound was added to the library.

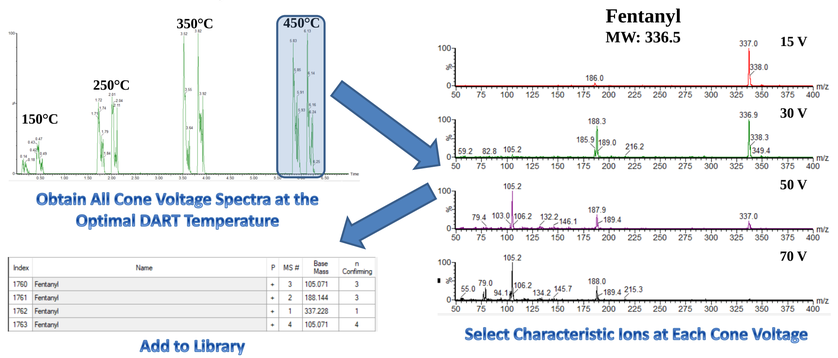


Figure 1: Workflow for creating the drug library.

Results

- A drug of abuse library and library search program have been created for targeted drug screening by DART-MS.
- The library currently contains **700** drug substances (Figure 2) with plans to be updated with an additional 800 substances for a total of 1500.

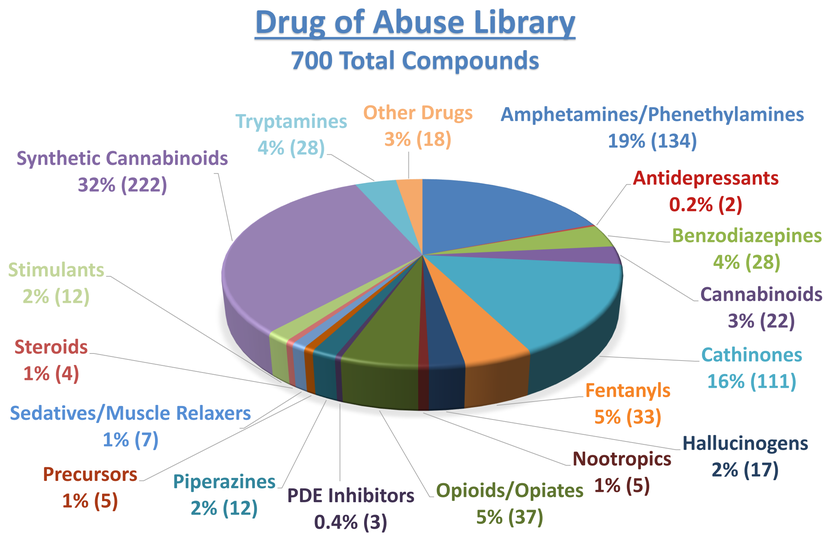


Figure 2: Current drug of abuse library containing 700 drug substances.

Reverse Library Search

- Identified alarming drugs displayed in a simple, red-colored oval shape where the size reflects the signal intensity of the drug (Figure 3).
- The library spectra and sample spectra comparison along with each detected analyte and its corresponding match probability are also displayed (Figure 3).

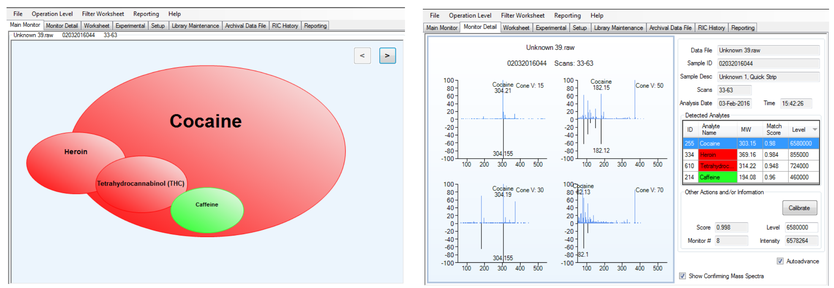
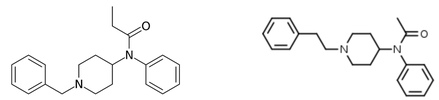


Figure 3: Simple display (left) and spectral comparison display (right) of identified compounds.

Differentiation of Isomers

- Certain constitutional isomers can be differentiated using in-source CID and reverse library search if fragmentation pattern is different.
- The skeletal isomers of benzyl fentanyl and acetyl fentanyl can readily be differentiated with in-source CID fragmentation (Figure 4).
- When searched against the library, the software program was able to differentiate the benzyl fentanyl from acetyl fentanyl (Figure 5).



Benzyl Fentanyl **Acetyl Fentanyl**

$C_{21}H_{26}N_2O$
MW: 322.5

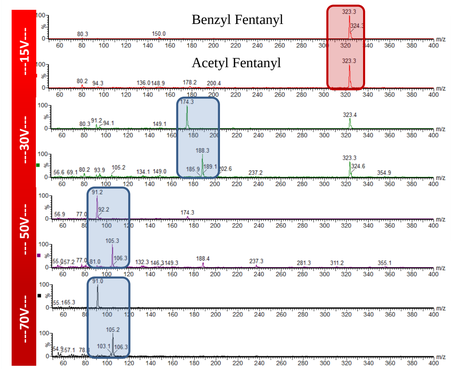


Figure 4: Differentiation of benzyl fentanyl and acetyl fentanyl with in-source CID fragmentation.

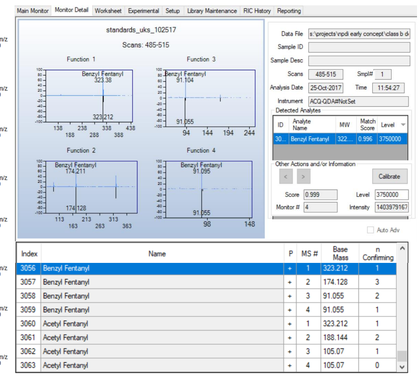


Figure 5: Benzyl fentanyl differentiated from acetyl fentanyl using the drug library and search algorithm.

Conclusion

- Cone voltages of 15, 30, 50 and 70 V, for this particular single quadrupole MS, provided sufficient precursor and fragment ion information to differentiate and identify 700 substances from various drug classes.
- The drug of abuse library created here can be used for accurate targeted drug screening.
- DART-MS in combination with reverse library search presents an attractive approach for rapid drug screening.

Future Work

- The current DART-MS drug library will be updated with an additional 800 substances, which will include the most up-to-date fentanyl-related compounds and other emerging drugs.