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Application News

Gas Chromatograph Mass Spectrometer GCMS-TQ™8050 NX

A Sample Prep-Free Analysis of Drug Molecules with "*Smart IS+*" and "*SMCI+*"

- Compound Identification -

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User Benefits

- "*Smart IS+*" and "*SMCI+*" setups direct qualitative GC/MS analysis of polar compounds such as drug molecules
- Choose between electron ionization and positive chemical ionization modes with "*Smart IS+*" setup or perform both ionization mode consecutively in a single GC/MS analysis
- Perform positive chemical ionization safely with "*SMCI+*" setup since it requires only common laboratory solvents as reagent gas

■ Introduction

The discovery and development of new drugs go through a series of lengthy processes that commonly begins in the synthetic laboratory. After the successful identification of a drug pharmacophore, the preparation of analogues demands a constant supply of starting materials. A rapid qualitative analysis method to confirm the successful synthesis of starting materials and thereafter the drug candidates would be important to increase the speed of drug discovery.

The usage of a direct probe as a sample inlet in GC/MS provides a rapid qualitative technique that eliminates the need for tedious sample preparation. It enables direct analysis of non-volatile, polar, and large molecules which typically requires multistep derivatization procedures for GC/MS analysis.

This article demonstrates the application of a direct probe in conjunction with a Smart EI/CI ion source (Smart IS) or solvent mediated chemical ionization (SMCI) unit for the analysis of drugs. The mass spectra of drug molecules generated by Smart IS and SMCI units will be evaluated.

■ Measurement Conditions and Samples

Analytical Setup.

The analytical results in this report were generated using a Direct Sample Inlet (DI) probe in conjunction with a Smart IS or SMCI unit. The combination of DI with Smart IS or SMCI unit is hence known as "*Smart IS+*" and "*SMCI+*" in this article, respectively (Fig. 1).

The DI probe is designed to be able to fit a miniature sample vial at its tip. The sample vial is thereafter placed close to the ion source and subsequently heated up according to a temperature program. The chemicals in the sample vial are hence volatilized and ionized in the ion source.

Smart IS is a 2-in-1 ion source that enables both electron ionization (EI) and positive chemical ionization (PCI) modes. PCI is achieved with the usage of isobutane gas as a reagent gas. Due to the simplicity of switching between two different ionization modes with Smart IS, the PCI mode attained with Smart IS is referred to as quick chemical ionization (QCI).

On the other hand, SMCI unit enables PCI mode with conventional PCI ion source and methanol as the reagent gas. Usage of methanol allows safe (i.e., it eliminates the use of flammable and toxic reagent gases such as methane, isobutane, and ammonia) and convenient adoption of PCI mode in routine GC/MS analysis.

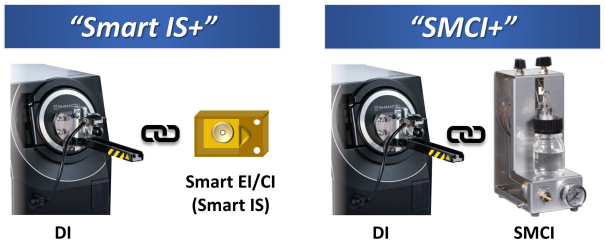


Fig. 1 *Polymode Ionization* setup inclusive of "*Smart IS+*" and "*SMCI+*".

A total of 7 drug molecules (Fig.2) from two different classes, specifically, nucleic acid (i.e., adenosine, inosine) and antibiotic (i.e., sulfamethazine, sulfamethoxazole, furazolidone, furaltadone, tazobactam) were analyzed here.

Experimental Condition.

Standard solutions of the drug molecules were prepared to a concentration of 5000 ppm in either water, acetone or DCM. 1 µL of each standard solution was introduced into individual DI sample vial for analysis. The samples were left to dry before analysis.

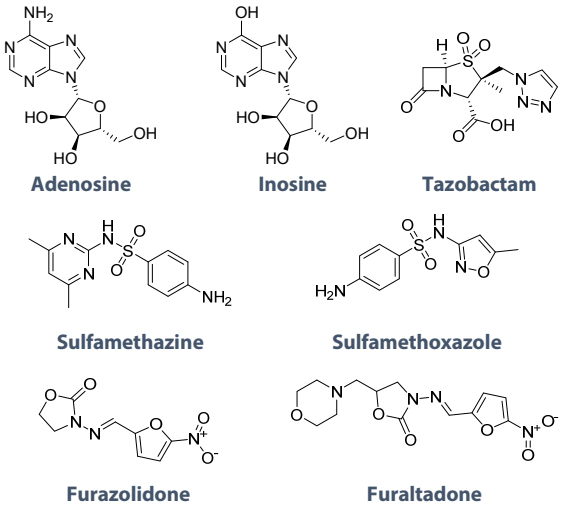
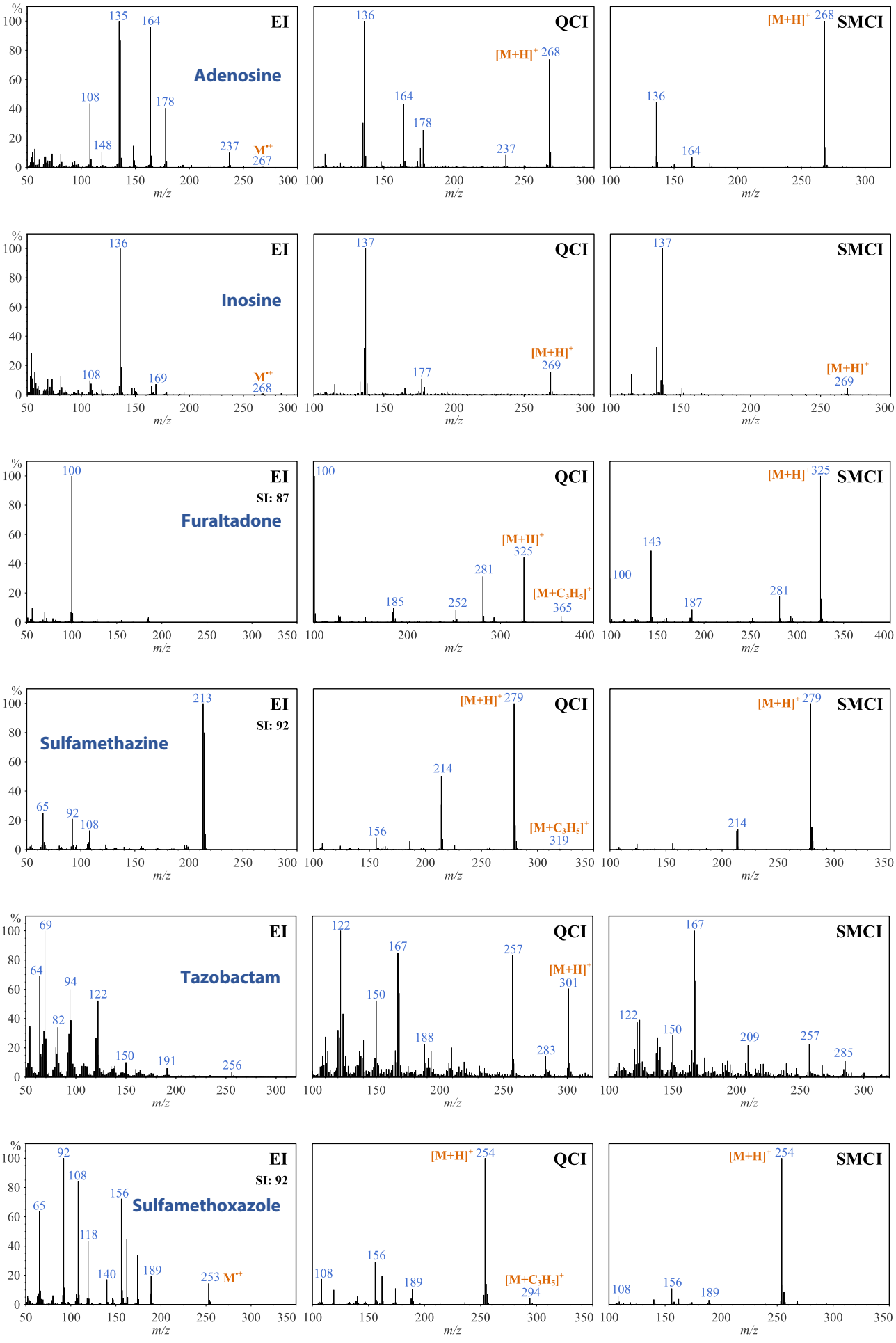


Fig. 2. Drug molecules.



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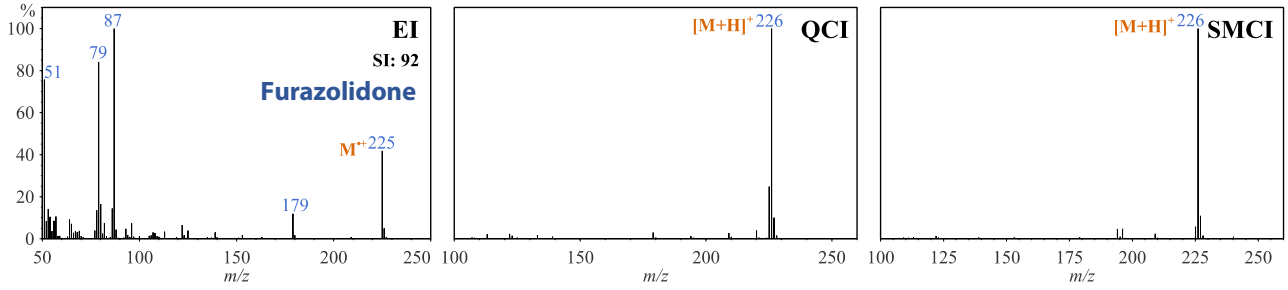

Fig. 3. EI, QCI, and SMCI mass spectra of adenosine, inosine, furaltadone, sulfamethazine, tazobactam, sulfamethoxazole and furazolidone. SI: Library similarity index.

The DI probe was heated at 20 °C /min to 100 °C, then 40 °C /min to 450 °C and held for 7 min. The ion source temperature was set to 230 °C. Ionization mode used included EI, QCI (isobutane), and SMCI (methanol). Scan mode was performed in the range of *m/z* 50-500 with a scan speed of 3333.

■ Results and Discussion

Mass Spectra of Nucleic Acids (Fig.3)

Adenosine and inosine consist of a ribose bonded via a glycosidic bond. The presence of ribose rendered the molecules highly polar but was nevertheless analyzed directly with the DI probe. The EI mass spectra were successfully collected but the intensities of the molecular ion peaks were barely visible.

When analyzed with QCI mode, the distinctive $[M+H]^+$ ion peak aid in the identification of the molecules. With SMCI mode, the $[M+H]^+$ ion peak of adenosine was the base peak while that of inosine was distinctive but low in intensity.

Mass Spectra of Antibiotics (Fig. 3)

Sulfamethazine, sulfamethoxazole, furazolidone, and tazobactam are antibiotics for humans while furaltadone is a veterinary drug.

The EI mass spectrum of furaltadone produced a clear fragment at *m/z* 100 without any molecular ion signal, despite attaining a similarity index score of >80 against the NIST mass spectral library. With QCI and SMCI mode, obvious $[M+H]^+$ ion peaks were observed, in which it appeared as the base peak in the latter.

Similarly, the molecular ion peak was not present in the EI mass spectrum of sulfamethazine, but the $[M+H]^+$ ion peak was distinctive in both QCI and SMCI mass spectra. As for tazobactam, the EI mass spectrum did not consist of the molecular ion peak. In contrast, analysis with QCI mode resulted in a distinctive $[M+H]^+$ ion peak at *m/z* 301. The $[M+H]^+$ ion peak was however not observed with SMCI mode.

While sulfamethoxazole and furazolidone produced EI mass spectra with obvious molecular ion peaks, both the QCI and SMCI mass spectra resulted in $[M+H]^+$ ion peak as the base peak. With high similarity index scores for the EI mass spectra, the additional $[M+H]^+$ ion peak information from the QCI and SMCI mass spectra further assisted in confirming their identities.

■ Conclusion

The "*Smart IS+*" and newly introduced "*SMCI+*" enable a direct and quick qualitative analysis of drug molecules. Analysis of polar drug molecules with GC/MS can be accomplished directly and without the need for tedious derivatization steps.

The "*Smart IS+*" setup delivers convenience in switching between electron ionization and positive chemical ionization mode of analysis. In addition, a consecutive switch between EI and QCI mode can also be achieved within a single GC/MS run. On the other hand, the "*SMCI+*" setup delivers utmost convenience and safety to carry out positive chemical ionization since it utilizes methanol, which is a common laboratory solvent, as the reagent gas.

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