Ion Source DUIS-2010 - Enabling even higher throughput analysis

Technical Report vol.10

1. Introduction

In the synthesis departments of pharmaceutical and chemical manufacturing enterprises, large numbers of compounds are synthesized and tested. Many LCMS instruments are running simultaneously in these fields, and this is where the “PsiPort Browser”, an LCMS software package that incorporates Web-based browser functionality, is actively being used to improve efficiency in research and development-related businesses (Reference: Technical Report No. 9). Although efficiency improvements using software can improve analysis throughput, software alone cannot improve the analysis itself. There is always the overriding question as to whether "the synthesized compounds are really being detected." Addressing this concern requires the application of new technology linked to the LCMS hardware itself.

2. Relationships between Ionization and Polarity and Molecular Weight

To clarify the problem facing LCMS today, let us focus on the ionization methods used in LCMS. Fig. 1 illustrates the relationship between the polarity and molecular weight of the target compound or analyte in LCMS analysis. The ideal ionization method will depend upon the physical properties of the compound to be analyzed by LCMS. As is evident from Fig. 1, there are three ionization modes, ESI, APCI and APPI modes, from which to select depending on the polarity of the compound. ESI and APCI are the most common techniques and are generally used for 95% or more of LCMS analyses. From the standpoint of thermodynamics, it is not going too far to say that the first approach to selection of the ionization mode in LCMS should be based on the physical properties of the compound. For example, the APCI mode is unsuitable for analysis of thermally unstable compounds.

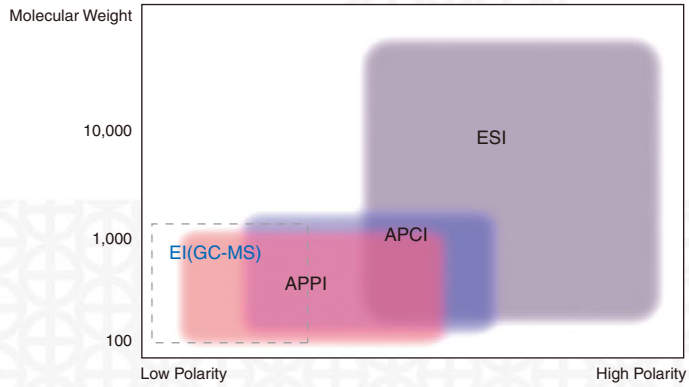


Fig. 1: Relationship Between Polarity, Molecular Weight and Ionization

Electrospray Ionization (ESI) is suitable for high-polarity compounds like pharmaceutical products and pesticides, while Atmospheric Pressure Chemical Ionization (APCI) is suitable for moderate polarity compounds such as steroids and low solubility drugs such as anticancer agents. Although a large number of compounds can be analyzed by any of these techniques, not all compounds produce the same ions, thus complicating the data interpretation. For example, ESI generally produces $[M+H]^+$ or $[M-H]^-$ ions, but occasionally produces $[M+Na]^+$ ions or $[2M+Na]^+$ ions. APCI also generally produces $[M+H]^+$ or $[M-H]^-$ ions, but occasionally produces $[M+solvent+H]^+$ or $[M]^+$ ions, so the ions are not always found at the expected mass. Synthesis researchers who are producing large numbers of compounds, may find it difficult to predict the best ionization method for a variety of samples.

To determine whether a synthesis reaction produced the desired target compound, pick the ionization technique that works best for that compound. The problem, however, is how to determine which technique to use. Each ionization approach can produce ions, but sometimes different ions. ESI normally produces $[M+H]^+$ or $[M-H]^-$ ions, but it might produce a sodium adduct or a dimer ion, at different masses than might be expected for the $[M+H]^+$ ion.

APCI might also produce a $[M+H]^+$ ion for many compounds, but it can also generate cluster ions with certain solvents, or might create ions with neutral mass losses of thermally labile compounds such as carbolic acids showing up at $[M-COOH]^-$ for example. So the question of whether the synthesized compound is detected or not can be complicated by the ionization technique used.

3. Can Both ESI and APCI Data be Acquired in a Single Analysis?

The key to resolving the problem is to use both techniques in a single analysis. This eliminates any concern regarding whether synthesized compounds are really being detected. Using both ionization mechanisms, with ESI forming ions first followed by APCI ionizing the remaining molecules, will result in the largest variety of compounds being ionized, and thus detected. However, a close look at the ESI and APCI ion sources reveals that the sources are different (see Fig. 2). The major difference between the ESI and APCI modes is that "there is a heater in the APCI ion source", or in other words, the sample is heated in the APCI mode, while it is not heated in the ESI mode. In order to acquire both ESI and APCI data in a single analysis, it is first necessary to resolve the problem of the hardware differences arising from the difference in ionization.

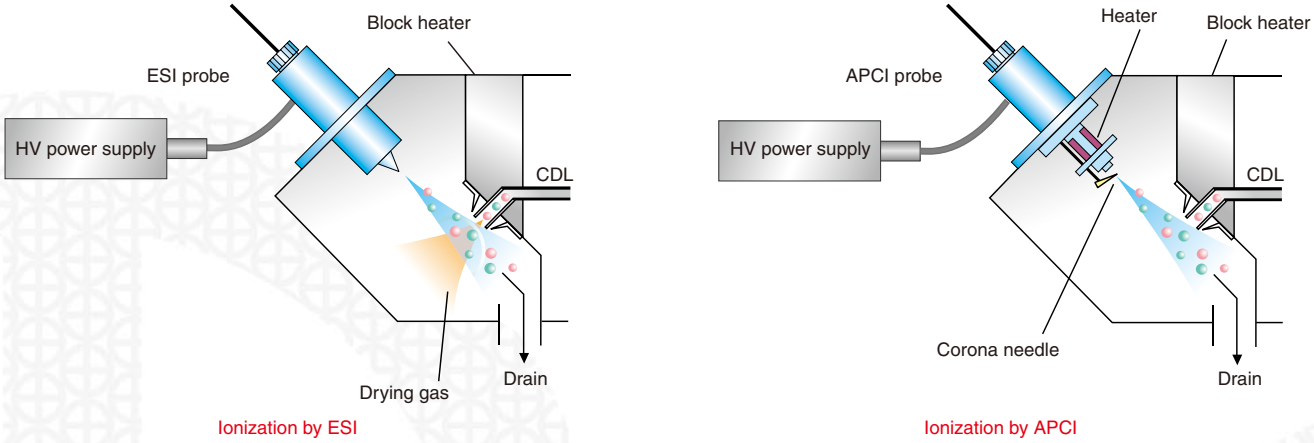


Fig. 2: ESI and APCI Mechanisms

4. Dual Ion Source DUIS-2010 for Simultaneous ESI and APCI Analysis

Dual Ion Source DUIS-2010 — the ion source that overcomes the ionization obstacles to allow acquisition of both ESI and APCI data in a single analysis, thereby enabling even higher throughput by synthesis research departments.

Here, let us review the ionization flow in the DUIS-2010 referring to Fig. 5.

1. Sample is introduced into the ESI probe.
2. Spray is formed and is atomized from the ESI probe.
3. ESI ionization occurs as the droplets evaporate.
4. Counter current drying gas heated to high temperature by block heater is used to dry the droplets.
5. Spray is volatized rapidly.
6. Volatilized gas is ionized by APCI reagent ions formed by a corona discharge.
7. Sample ionized by ESI and APCI is introduced into MS.

As described in this section, it is clear that simultaneous analysis is possible with the DUIS-2010. Moreover, because there is no switching of ionization modes in the DUIS-2010, so there are no missed peaks, and the source is compatible with fast HPLC.

The DUIS-2010 provides ionization of a wide range of compounds, from low polarity to high polarity compounds. Of course, positive/negative polarity switching is also supported, demonstrating the power of the DUIS-2010 in such applications as multi-component synthesis and impurity evaluation. Furthermore, the ion source construction is extremely simple, as shown in the photograph of Fig. 5, so maintenance is easy.

Fig. 3: LCMS-2010EV + DUIS-2010

Fig. 4: External View of DUIS-2010

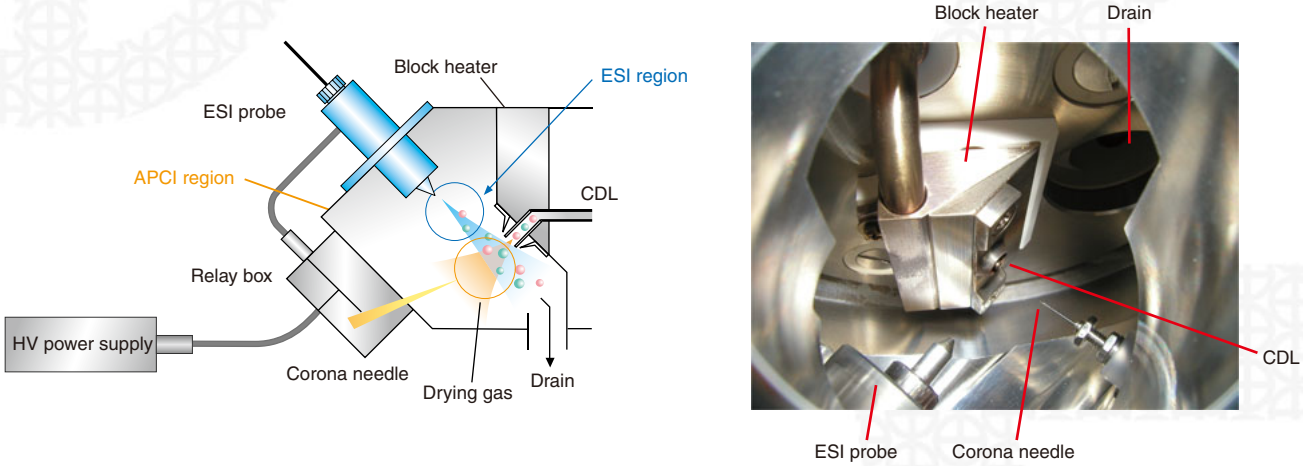


Fig. 5: DUIS-2010 Structural Diagram and Photo of Interior

5. Higher Throughput Efficiency with DUIS-2010

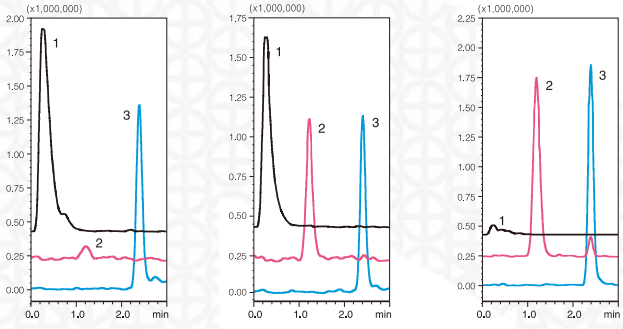
Here we introduce an example of analysis using the DUIS-2010. Fig. 6 shows the mass chromatograms obtained from analysis of a sample mixture containing streptomycin, acetophenone and butyl paraben, each obtained using a different ion source. As can be seen in the figure, excellent response is obtained for streptomycin (peak 1) using the ESI ion source, as would be expected because it yields a protonated molecule. However, using the APCI ion source, it is just barely detected.

With respect to peak 2, acetophenone, the protonated molecule is detected using the APCI ion source, but ionization is inadequate with the ESI ion source. In contrast, when the dual ion source is used, a well-balanced mass chromatogram is obtained.

In addition, by conducting simultaneous positive/negative analysis, the constituent yielding the deprotonated molecule butyl paraben, peak 3, is also clearly detected.

On the other hand, Fig. 7 shows the mass spectrum of butyl paraben obtained using each of the ion sources. Butyl paraben mainly generates a deprotonated molecule with both the ESI and APCI ion sources. With the dual ion source also, a deprotonated molecule similarly becomes the base peak, so that the molecular weight is easily verified.

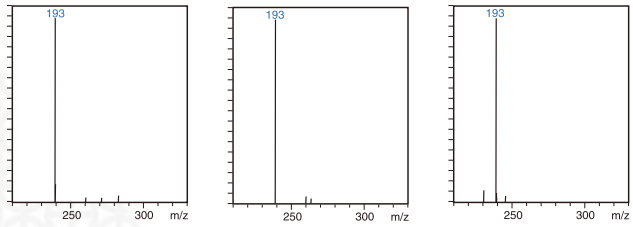
Thus, we were able to demonstrate high throughput analysis using the DUIS-2010. Use of the DUIS-2010 simplifies all aspects of LCMS detection.



ESI Ion Source | Dual Ion Source | APCI Ion Source

1. Streptomycin $[M+H]^+$ m/z 582
2. Acetophenone $[M+H]^+$ m/z 121
3. Butyl paraben $[M-H]^+$ m/z 193

Fig. 6: Mass Chromatograms Using Each Ion Source



ESI Ion Source | Dual Ion Source | APCI Ion Source

Fig. 7: Mass Spectra Using Each Ion Source

6. Achieving True High Throughput in Combination with Prominence UFLC

Along with high throughput analysis in vogue now, the “quality of analysis” has also come to be expected. The Prominence UFLC ultra fast liquid chromatograph and the ultra-high-speed, high resolution XR-ODS column are a hardware and column combination that emerged to satisfy the demand for high speed, and are already in routine use.

Ultra-high speed has not stopped at LC analysis, but has extended to LCMS analysis, as well. The combination of the Prominence UFLC and XR-ODS with the LCMS-2010EV will provide for even greater gains in analysis speed. The combination of an ultra-high-speed HPLC system with the simultaneous ESI/APCI capabilities of the DUIS-2010 source provides the ultimate performance, throughput and simplicity.

Fig. 8 shows an example of high-speed analysis of N-methyl carbamate pesticides, and Fig. 9 shows the repeatability data of the pesticide methomyl. From this it is clear that combining the LCMS-2010EV and Prominence UFLC provides ultra-high-speed separation while maintaining extremely high accuracy, with area repeatability of 1.2%.

As described above, the DUIS-2010 is an ion source that enables even higher throughput, and true high throughput was achieved using it in combination with the Prominence UFLC and XR-ODS.

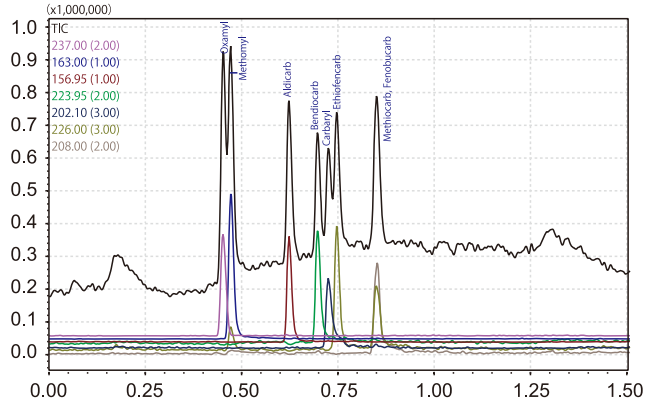


Fig. 8: High-Speed Analysis of N-Methyl Carbamate Pesticides Using Combination of Prominence UFLC and DUIS-2010

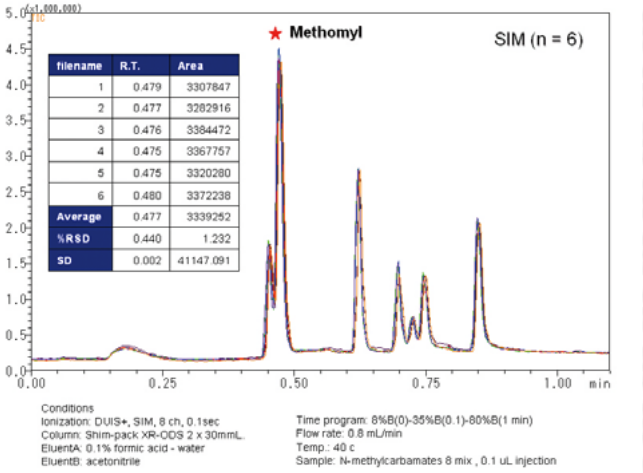


Fig. 9: Methomyl High-Speed Analysis Chromatogram Repeatability Using Combination of Prominence UFLC and DUIS-2010

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