Smiths Detection

Ion Mobility Spectrometry (IMS): An Alternative to HPLC for Cleaning Validation

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IONSCAN®-LS Ion Mobility Spectrometers provide trace analysis with the advantages of minimal sample preparation, simplicity of use, high sensitivity, fast results, and low operating cost. The advantages of this technique include: minimal sample preparation, simplicity of operation, sub-nanogram sensitivity, atmospheric pressure operation, rapid analysis, 5-20 s per analysis and sample throughput of up to 60 samples/h. This technology has been applied in the pharmaceutical and chemical markets for cleaning validation, raw material identification and quality control.

Ion mobility spectrometry (IMS) characterizes chemical substances based on their gas-phase ion mobilities and provides detection and quantitation of trace analytes. IMS instruments consist of a sample introduction system, an ionization source, an analyzer for separating ions according to their ion mobilities, a detector, and a computer for instrument control and data acquisition.

This technique can directly analyze solid, liquid or gaseous samples. The sample is carried into the ionization region of the IMS by a flow of an inert gas such as dried air. Sample ionization is accomplished by atmospheric pressure chemical ionization (APCI) using a ^{63}Ni source. The IMS analyzer may be operated in either positive or negative ion detection mode.

An electronic gate opens periodically, typically for 200 µs every 20-30 ms, to admit a pulse of product ions into the drift tube. The ions drift downfield under the influence of a controlled electric field against a counter-flow of an inert drift gas at ambient pressure towards a detector. Collisions and interactions with the drift gas retard the flow and separate the ions. Lighter, smaller ions have greater ion mobility and, hence, exhibit shorter drift times. Thus, ions separate according to chemical identity as they traverse the drift region. The ion current at the detector is amplified and displayed as a plasmagram, showing ion current vs. drift time, as shown in Figure 1.

Quantitative information may be obtained by analyzing the amplitude or area of an ion peak that derives from the sample compound. Comparison to a standard curve is generally performed.

Results

Selectivity/Specificity:

- Specificity is excellent. Peak locations are determined to within 50 µs.

Sensitivity:

- Typical limits of quantitation are between 0.1 and 5 ng.

Linearity:

- R^2 (correlation coefficients) generally exceed 0.99.

Precision:

- RSDs range from 1-5%.

Data Interpretation:

- Limit test can provide pass/fail answers.
- Linear calibration yields quantitative information.

Sample Throughput:

- Up to 60 samples/h.

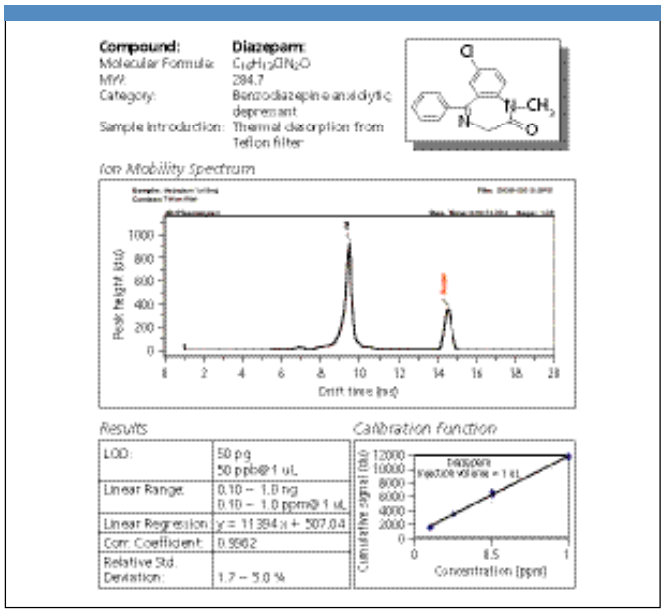

Figure 1: IonScan compound characterization.

*Partial List of Active Pharmaceuticals Characterized by IONSCAN-LS®-LS**

Acetaminophen	Flurazepam	Oxycodone
Acetylsalicylic Acid	Glucosamine-HCl	Pentobarbital
Alprazolam	Haloperidol	Phenobarbital
Amitriptyline-HCl	Hydrocodone	Procaine
Amobarbital	Hydromorphone	Ranitidine
Amphetamine	Ibuprofen	Salicylic Acid
Antipyrine	Imipramine-HCl	Secobarbital
Benzocaine	Indomethacin	Sertraline
Butalbital	Ketamine	Tamoxifen
Chlordiazepoxide	Lidocaine	Temazepam
Chlorpheniramine	Lorazepam	Theophylline
Clonazepam	Manitol	Tramadol
Clonidine	Methadone	Triazolam
Cocaine	Methamphetamine	Trimipramine Maleate
Codeine	Morphine	
Diazepam	Nicotine	*Limits of Quantitation are generally 0.1-5 ng.
Ephedrine	Noscapine	
Fentanyl	Methohexital	
Flunitrazepam	Oxazepam	

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