MAYO CLINIC
Mayo Medical Laboratories

THE MML DIFFERENCE:
MASS SPECTROMETRY

BACKGROUND

A mass spectrometer (MS) measures the weight of ions derived from neutral compounds after ionization. Generated ions are separated based on their mass-to-charge ratio and a recorder plots the mass-to-charge ratio values, normalized as the percentage of the most abundant species in the sample, ie, a mass spectrum (Figure 1). The height of each ion peak in the mass spectrum correlates to the abundance of each ion in the original sample and allows for qualitative interpretation of the ion profile. Quantitative determination of the concentration of specific ions is made possible by the addition of defined concentrations of internal standards.

Tandem mass spectrometers (MS/MS) consist of two mass spectrometers coupled in series and separated by a collision cell. The first MS analyzes the ions in a sample (pre-cursor or parent ions). The precursor ions are then fragmented in the collision cell by use of an inert gas. The product ions (or daughter ions) resulting from fragmentation are further analyzed by the second MS. The first or second MS can be set either to scan a mass range or to select one or more individual ions of a specific mass-to-charge ratio.

MS allows the analysis of individual compounds in complex mixtures. Assessment of the profile and comparison to patterns generated by known compounds allow quantification and/or characterization of the sample's constituents.

MS can be combined with other methods to improve detection and sensitivity. These combinations, such as inductively coupled plasma MS (ICP/MS),* gas-chromatography MS (GC-MS), and liquid chromatography-MS/MS (LC-MS/MS) methods, are used for

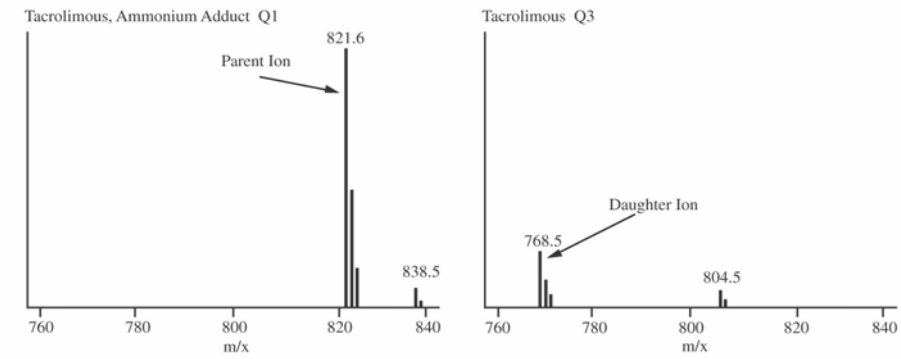

Figure 1: Mass Spectrum

many tests offered by Mayo Medical Laboratories including acylcarnitines, newborn screening, organic acids, therapeutic drug monitoring, trace element monitoring, hormones, homocysteine, and homovanillic acid.

TECHNOLOGICAL COMPARISON

MS relies on direct physical measurement of the analyte to generate the report signal and it is, therefore, a **reagentless** technology.

- Reagentless technology largely eliminates** dependence on manufacturers' products and their subsequent lot-to-lot and vendor-to-vendor variability:
  - Improves precision.
  - Reduces supply costs.
- Direct measurement is superior to indirect methods (eg, immunoassay methods, which determine the amount of analyte present by measuring antibody binding and are prone to interferences) and:
  - Improves accuracy and precision.
  - Eliminates false-positive and false-negative results due to interferences.
- Sensitivity better or equal to the best immunoassays.
- Unsurpassed specificity.
- Multiple analytes measured in a single specimen.
- State-of-the-art-technology.
- Rapid, high throughput systems.
- Small specimen volume requirements (sample volumes of usually <100 µL).

Mayo was the first to develop and offer clinical MS/MS applications and continues to lead in this field. Mayo's wide application of the MS technologies to clinical testing has enabled our consultants to acquire significant experience in the development of MS tests and interpretation of test results. Mayo performs over 300,000 MS tests each year utilizing MS technology in metals analysis, biochemical genetics, toxicology, and other areas.

PATIENT CARE INFORMATION

MS has made it possible to accurately and precisely detect and quantify numerous analytes cost-efficiently. MS results in increased accuracy in diagnosis and more efficient monitoring of patients and disease processes. Ongoing conversion to MS-based technology is a high priority for Mayo, supporting improved patient care.

REFERENCES

1. Matern D, Magera MJ: Mass Spectrometry Methods for Metabolic and Health Assessment. J Nutr 2001;131:1615S-1620S
2. Rinaldo P, Hahn SH, Matern D: Inborn errors of amino acid, organic acid, and fatty acid metabolism. In Tietz Textbook of Clinical Chemistry, 4th edition. Edited by CA Burtis, ER Ashwood, NW Tietz. WB Saunders 2004: in press

*In ICP-MS, plasma (ie, a gas containing of ions, electrons and neutral particles) is used to atomize and ionize the elements in a sample. The ionized gasses plus neutral species are aspirated from the plasma through an orifice into a quadrupole mass spectrometer.

** Internal standards, columns, etc, required.