

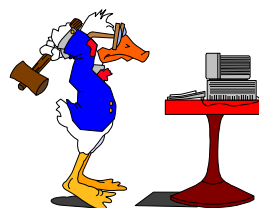
Pharmacy 325

Mass Spectrometry (MS)

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Hours: anytime after 4 pm

Lecture Notes Available At:

- <http://redpoll.pharmacy.ualberta.ca>
- <http://www.pharmacy.ualberta.ca/pharm325/>



Mass Spectrometry

- Uses the interaction of electric and/or magnetic fields (i.e. electromagnetic radiation) with matter to determine weight or mass
- Measures mass, not absorption or emission of electromagnetic radiation

MS History

- Concept first put into practice by Francis Aston, a physicist working in Cambridge England in 1919
- Designed to measure mass of elements (esp. isotopes)
- Awarded Nobel Prize in 1922
- Now one of the **MOST POWERFUL ANALYTIC TOOLS IN CHEMISTRY**

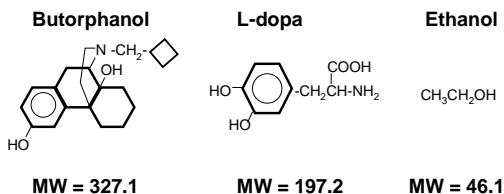
MS Principles

- Different elements can be uniquely identified by their mass



MS Principles

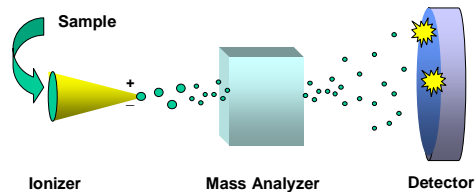
- Different compounds can be uniquely identified by their mass



MS Principles

- Find a way to “charge” an atom or molecule (ionization)
- Place charged atom or molecule in a magnetic field or subject it to an electric field and measure its speed or radius of curvature relative to its mass-to-charge ratio (mass analyzer)
- Detect ions using microchannel plate

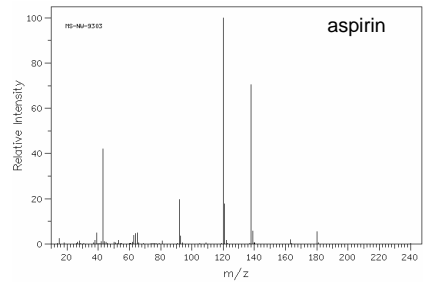
Mass Spec Principles



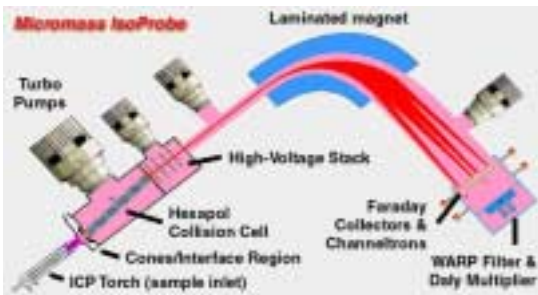
Typical Mass Spectrometer



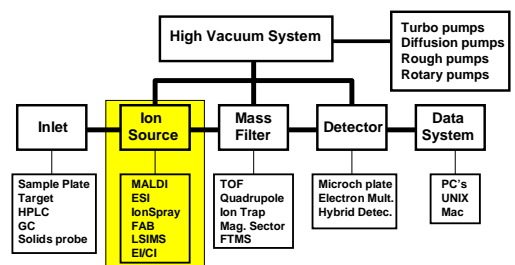
Typical Mass Spectrum



Inside a Mass Spectrometer

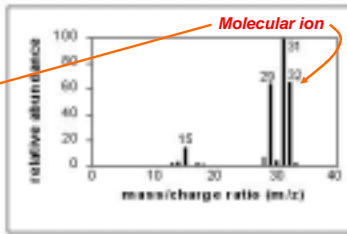


Mass Spectrometer Schematic



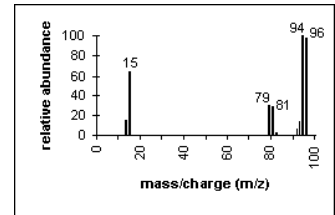
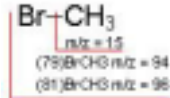
Electron Impact MS of CH₃OH

ions	m/z
CH ₃ OH ⁺	32
H ₂ C=OH ⁺	31
HC=O ⁺	29
H ₂ C ⁺	15



EI Breaks up Molecules in Predictable Ways

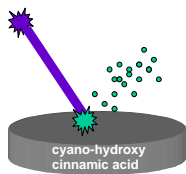
Electron Impact MS of CH₃Br



Isotopes can help in identifying compounds

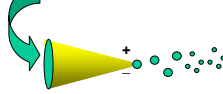
Soft Ionization Methods

370 nm UV laser



MALDI

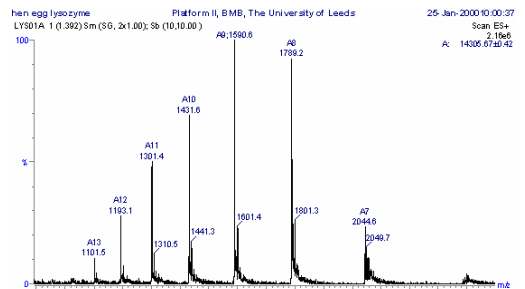
Fluid (no salt)



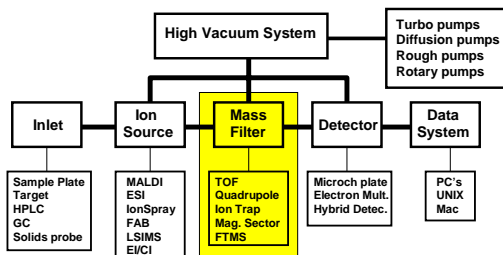
Gold tip needle

ESI

Multiply Charged Ions



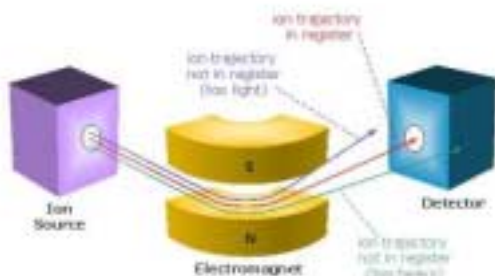
Mass Spectrometer Schematic



Different Types of Mass Analyzers

- **Magnetic Sector Analyzer (MSA)**
 - High resolution, exact mass, original MA
- **Quadrupole Analyzer (Q or Q*)**
 - Low (1 amu) resolution, fast, cheap
- **Time-of-Flight Analyzer (TOF)**
 - No upper m/z limit, high throughput
- **Ion Cyclotron Resonance (FT-ICR)**
 - Highest resolution, exact mass, costly

Magnetic Sector Analyzer

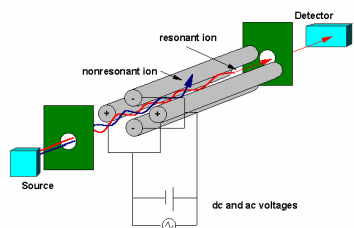


The Mass Spec Equation

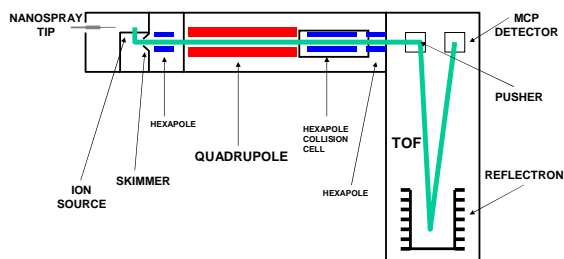
$$\frac{m}{z} = \frac{B^2 r^2}{2V}$$

M = mass of ion **B** = magnetic field
z = charge of ion **r** = radius of circle
V = voltage

Quadrupole Mass Analyzer



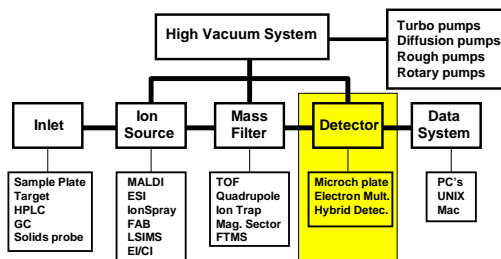
Q-TOF Mass Analyzer



FT-Ion Cyclotron Analyzer



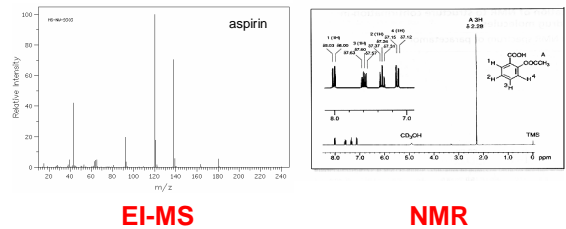
Mass Spectrometer Schematic



MS Detectors

- Early detectors used photographic film
- Today's detectors produce electronic signals when struck by an ion
- Timing mechanisms integrate these signals with scanning voltages to allow the instrument to report which m/z has struck the detector
- Need constant and regular calibration

MS vs NMR



MS vs. NMR

- MS peaks are narrower than NMR peaks
- MS is much more (10^4 x) more sensitive than NMR (**among most sensitive tools**)
- MS allows one to analyze much larger molecules (>50 kD) than NMR
- MS samples are more difficult to prepare
- MS is not particularly quantitative
- MS instruments cost a little less than NMR

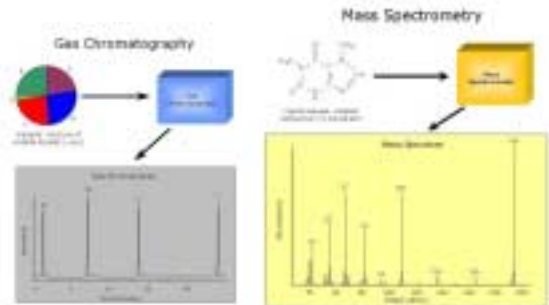
Different Types of MS

- **ESI-QTOF**
 - Electrospray ionization source + quadrupole mass filter + time-of-flight mass analyzer
- **MALDI-QTOF**
 - Matrix-assisted laser desorption ionization + quadrupole + time-of-flight mass analyzer

Different Types of MS

- **GC-MS - Gas Chromatography MS**
 - separates volatile compounds in gas column and ID's by mass
- **LC-MS - Liquid Chromatography MS**
 - separates delicate compounds in HPLC column and ID's by mass
- **MS-MS - Tandem Mass Spectrometry**
 - separates compound fragments by magnetic field and ID's by mass

GC-MS



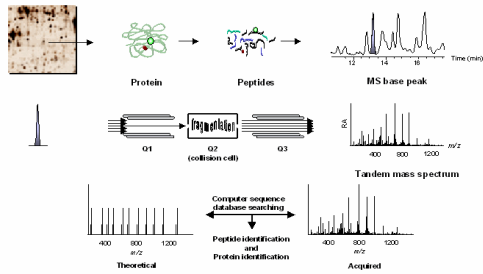
Gas Chromatography

- Sample (must contain stable, volatile compounds) is vaporized in a heated chamber
- Column is filled with silanized (silicon-coated) calcium silicate
- Column is kept hot (400 °C) in oven
- Sample is pushed through column using gas pressure (He or N₂)

Applications

- Determination or confirmation of chemical structure of drugs and drug metabolites (**MS-MS**)
- Detection/quantitation of impurities
- Detection/quantitation of drugs and their metabolites in biofluids and tissues
- High throughput drug screening
- Analysis of liquid mixtures (**LC-MS**)

Mass Spec & Proteomics



Other Applications

- **Clinical testing (detection of inborn errors of metabolism, cancer, diabetes, organic solvent poisoning, drugs of abuse, etc. etc.)**
- **Fingerprinting nutraceuticals and herbal drugs**
- **Fingerprinting or tracing source of natural products or drugs (Isotecnika)**