MASS SPECTROMETRY

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1 INTRODUCTION

The intent of this chapter is to provide a concise summary of informative topics related to the study of therapeutic agents by mass spectrometry (MS). Due to the vast number of published studies in this field alone, we have elected to restrict the cited literature to only the most recent as possible. Our objective is to highlight as many pertinent MS techniques as possible. However, it should be noted that this will not be an all-inclusive list of approaches due to the large volume of literature. Additionally, our intent is not to emphasize equations and detail about theory; a plethora of textbooks, training manuals, and journal articles concerning these details already exists. Theory will be discussed and referenced in this work only when its integration can make points more understandable.

This chapter is primarily divided into the areas of instrumentation, sample preparation, and applications in proteomics, metabolomics, and emerging fields in drug analysis. Each division will be discussed using examples from recent literature with the expectation that the reader will navigate to the appropriate topic for explanations and for direction to relevant citations. More time will be spent on instrumentation details in the first part in order to build a solid platform on which to discuss relevant applications in the latter portion of this review. Moreover, specific mass spectrometer designs used in the development and analysis of therapeutic agents will be given more attention based on their relevance and abundance in the literature.

2 INSTRUMENTATION

2.1 Sample Purification

In general, most MS experiments are easiest and results most accurate when a sample is as homogeneous as possible. Otherwise, the interpretation of mass spectra becomes less trivial, for example, when dealing with multiple-charge peaks in an electrospray ionization (ESI) experiment. Although software for deconvoluting ESI mass spectra accompanies most if not all commercial mass spectrometers nowadays, the software is usually unable to determine sample purity. The software attempts to identify the most probable protein(s) based on mass spectral comparison between experimental and theoretical data.

There are numerous methods employed in the fractionation, desalting, and specific selection (binding) of sample components prior to analysis and detection by MS. We will discuss several forms of sample treatment that make the analysis of pharmaceuticals and related drugs possible by MS.

High-Performance Liquid Chromatography High-performance liquid chromatography (HPLC), also known as high-pressure liquid chromatography, is the most widely used (online) method of sample separation for analysis by MS. HPLC is so commonly used that, at the time of this writing in July 2011 when we executed a Scifinder Scholar [1] search (criteria: *dates 2003–2011, journal only, English language*), almost 95,000 hits were

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