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GLYCOPINION

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Structure determination occupies a key position in modern glycobiology and has been greatly facilitated in recent years by developments in enzymology, chromatography, NMR and mass spectrometry (MS). Structural analysis of carbohydrates presents greater problems than that of other biomolecules such as oligonucleotides or proteins because of the complexities introduced by branching, linkage and anomericity. Consequently, it has not yet reached the advanced, and sometimes automated, state achieved in these other areas. Nevertheless, considerable progress has been made in recent years, although no single (MS) technique can yet provide all the necessary information.

High sensitivity is an essential requirement for any method of structural analysis as the quantities of oligosaccharide available are generally low. Biological techniques, such as selective cleavages of radiolabelled sugars with specific exoglycosidases, possess the necessary sensitivity and have been the preferred methods to date. However, even though some progress is being made towards automation, these classical sequencing techniques are frequently tedious and time consuming. Physical and chemical techniques, on the other hand, are generally more rapid and may eventually provide the answer to the problem of automating the structural determination of oligosaccharides. Mass spectrometry appears to be particularly promising in this respect as it possesses the ability to yield considerable structural information on very low (pmol–fmol range) concentrations of sample.

This article, by David Harvey, explores the use of both classical and modern mass spectrometry as applied to oligosaccharide analysis and addresses such questions as:

- Will mass spectrometry soon become the most powerful physical analytical technique in oligosaccharide analysis?
- Which mass spectrometric techniques are suitable for on-line coupling to affinity chromatography and capillary electrophoresis and, conversely, which chromatographic techniques are most appropriate for coupling to mass spectrometry?
- When is derivatization necessary?
- Can fragmentation be controlled?
- Can mass spectrometry be used to fingerprint glycoform libraries?
- How sensitive are the different techniques?
- Which technique is best for monosaccharides and which for glycoconjugates?

MINI-REVIEW

The role of mass spectrometry in glycobiology

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Mass spectrometry originated early in this century with the classic work of scientists such as Aston and Thompson [1], and led to the discovery of stable isotopes, thus allowing the nonintegral masses of the elements to be rationalized. However, it was several decades after the initial discovery before the technique was applied to the structural analysis of organic molecules. Even then, it was largely restricted to analysis of hydrocarbons from petroleum, mainly because of their volatile and thermally stable properties. The coupling of mass spectrometry with gas chromatography (GC) [2], the introduction of chemical derivatization for stabilization of thermally unstable molecules, and the development of efficient data processing systems were the key steps in the extension of the technique to biomolecule analysis. GC/MS proved to be particularly useful and is now a major technique in areas such as lipid and drug metabolite analysis. The coupling of liquid chromatographs and the extension of the mass range accessible by mass

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