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Applications of the Reaction Interface/Mass Spectrometer Technique to the Analysis of Selected Elements and Nuclides from Submicrogram Quantities of Biological Macromolecules and Xenobiotics

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Markey and Abramson [1] developed a microwave-powered chemical reaction interface, a device which converts a complex organic molecule in the presence of a reactant gas into small stable molecules which are detected by mass spectrometry. For a given reactant gas the molecules formed are a representation of the elemental composition of the original anlayte. The combination of the reaction interface and a mass spectrometer produces an isotope- or element-selective detector for samples either introduced directly into the reaction interface or flowing from a capillary gas chromatograph column.

Microgram and submicrogram samples of a variety of proteins were analyzed for their sulfur content relative to their carbon content by introducing the samples directly into the reaction interface. With CO_2 as the reactant gas, SO_2 at m/z 64 is produced. This quantifies the amount of sulfur which was introduced into the reaction interface. In the presence of N_2, HCN at m/z 27 is produced and is used to quantify the carbon content of the sample. The observed ratio of S/C for various proteins correlated well with the elemental formulas [2].

In the presence of SO_2, ^{14}NO at m/z 30 and ^{15}NO at m/z 31 are produced. Following administration of 50 mg of triple-labeled 5,5-diphenylhydantoin [1, 3(^{15}N); 2(^{13}C)] to a male beagle dog, a urine sample was selectively analyzed for its ^{15}N content by capillary gas chromatography—reaction interface/mass spectrometry. The corrected ratio of m/z 31 to m/z 30 produced a highly selective chromatogram showing only peaks of ^{15}N enrichment. Mass spectra of these peaks were obtained which permitted identification of phenytoin and several of its metabolites.

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References

[1] Markey, S. P., and Abramson, F. P., J. Chromatogr. **235**, 523 (1982).
[2] Abramson, F. P., and Markey, S. P., Biomed. Env. Mass Spectrom. **13**, 411 (1986).

Alkylation of DNA In Vivo: Development of Analytical Methodology for Trace Quantitative Analysis

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1. Abstract

The application of tandem MS techniques to the determination of the site and extent of alkylation of DNA by chemical carcinogens is illustrated. It is shown that it is possible to i) separate many methyldeoxyribonucleosides and the common deoxyribonucleosides in a single LC run, ii) detect and quantify pure methyldeoxyribonucleosides at the 10^{-14} mole level by desorption chemical ionization tandem mass spectrometry, and iii) quantify the major methylated nucleosides resulting from treatment of calf thymus DNA or hamster V79 cells with methylnitrosourea (MeNU) or methylmethanesulfonate (MeMS). The ultimate aim is to use *in vivo* experiments to correlate mutagenicity and cytotoxicity of the alkylating agents with the type and distribution of the alkylated adducts and with their metabolic half-lives (metabolic persistence/repair) in cell cultures.