Drug Discovery Accelerates as Metabolite Analysis Improves

Gérard Hopfgartner

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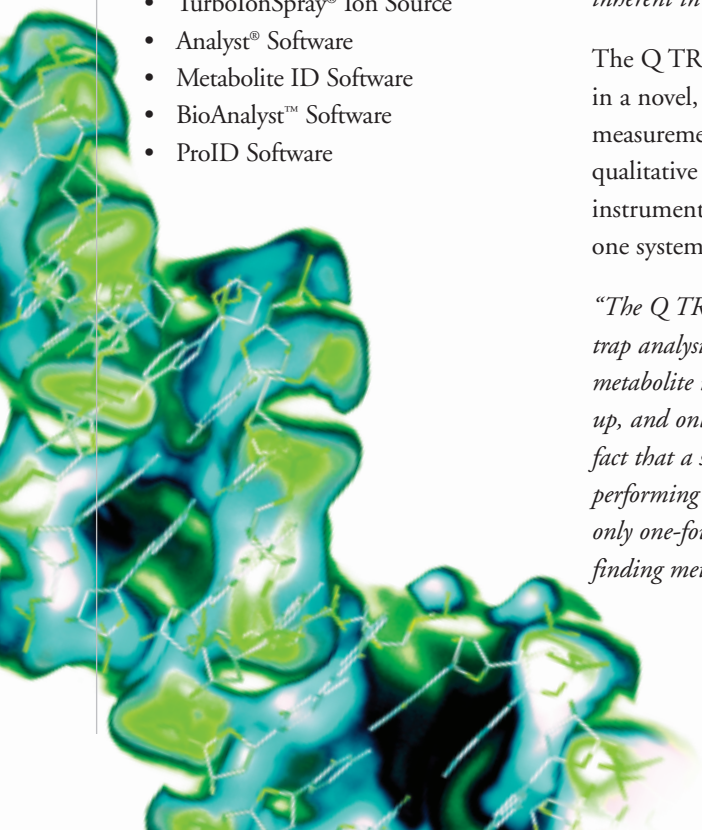
Application

- Drug Development
- ADME Studies

Applied Biosystems Technology:

- Q TRAP™ LC/MS/MS System
- TurboIonSpray® Ion Source
- Analyst® Software
- Metabolite ID Software
- BioAnalyst™ Software
- ProID Software



Gérard Hopfgartner is a professor of pharmaceutical analytical chemistry at the University of Geneva. A long-time mass spectrometrist, Prof. Hopfgartner and colleagues study different mass spectrometry (MS) techniques for qualitative and quantitative analysis of pharmaceuticals and their metabolites in biological samples. These analyses measure organism-drug interaction, including the degree of metabolic uptake, activity in the body before breakdown, production of toxic metabolites, and excretion or storage of the drug and its products. The results are key to determining the drug's potential for further development.

"Until now, characterization of metabolites required several different types of mass spectrometers and often duplicate analyses to ensure accuracy," Prof. Hopfgartner said. Traditionally done by LC/MS, inconsistent chromatographic conditions often necessitated multiple analyses to ensure results, contributing to an already costly and labor-intensive process.

These obstacles have been overcome by the Q TRAP™ LC/MS/MS system from Applied Biosystems/MDS SCIEX. *"Our results on projects for a major pharmaceutical company and at the university show that we can reduce the time required to screen and identify metabolites by a factor of three or four while gaining the cost reductions inherent in replacing two instruments with one,"* Prof. Hopfgartner states.

The Q TRAP system combines triple-quadrupole and ion trap mass spectrometers in a novel, hybrid configuration. While a triple-quad MS excels at quantitative measurement (how much analyte is present in a sample), the ion trap excels at qualitative screening (what analytes a sample contains). With the Q TRAP hybrid instrument, researchers can get sensitive quantitative and qualitative analysis in one system.

"The Q TRAP system is unique in that its ability to perform triple quadrupole and ion trap analysis on a single sample dramatically reduces the time required for metabolite identification," Hopfgartner reports. *"Only one instrument needs to be set up, and only one sample needs to be prepared. Additional improvements come from the fact that a single sample is used for multiple analyses. This eliminates the need for performing duplicate LC/MS runs. The result is that metabolites can be identified in only one-fourth to one-third the time that conventional methods require. We are now finding metabolites in much less time, using much less sample."*

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Because of the time, labor, and cost, metabolite screening and quantitation have typically been performed in pre-clinical and clinical phases of drug development. The faster, simpler, more affordable analysis the Q TRAP system provides may enable pharmaceutical companies to move this process to earlier phases of the drug development process, and help them determine the best candidates for their costly pre-clinical and clinical trials.

Prof. Hopfgartner uses the Q TRAP system for both small molecule and proteomics applications. For small molecule analysis, the system includes Metabolite ID and Analyst® software, and the TurboIonSpray® ion source and atmospheric pressure chemical ionization (APCI) source. For proteomics applications, the system includes ProID (protein identification) and BioAnalyst™ software, and the TurboIonSpray® and NanoSpray™ ionization sources.

The selective triple quadrupole filtering functions, precursor ion, and neutral loss scans of the Q TRAP system help with data reduction. *"What's important in science is not just to generate data, but to generate relevant data,"* Hopfgartner notes. Traditionally proteomics studies produce massive amounts of data, and use bioinformatics software to filter it. The Q TRAP system provides data reduction at the front end. *"It's like radar, so that I see only things which are relevant for my work."*

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