Agilent METLIN Personal Metabolite Database and Library

MORE CONFIDENCE IN COMPOUND IDENTIFICATION

The Measure of Confidence

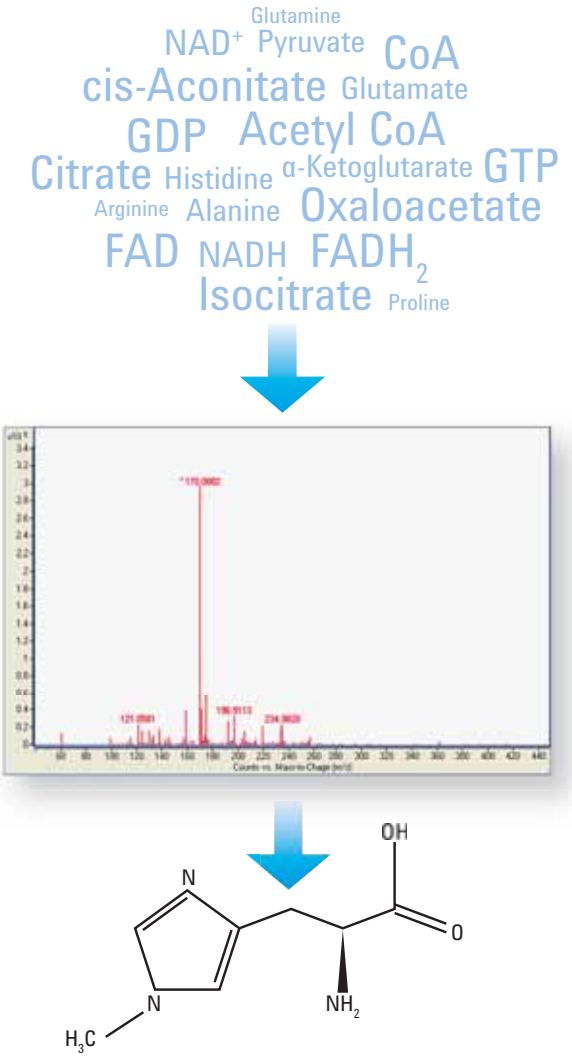
Agilent Technologies

COMPOUND IDENTIFICATION AT YOUR FINGERTIPS

Compound identification is a key element in untargeted metabolomics experiments aimed at understanding the global metabolic changes that can occur in a biological system. The confidence level in identification is directly dependent on the quality of the database used. The METLIN metabolite database, created by Dr. Gary Siuzdak, is one of the most comprehensive and widely used metabolite databases in the world today. It includes masses, chemical formulas, and structures for over 25,000 endogenous and exogenous metabolites, lipids, and di- and tri-peptides.

Agilent Technologies is the exclusive provider of the **METLIN Metabolite Personal Compound Database (PCD)** and the **METLIN Metabolite Personal Compound Database and Library (PCDL)**, which reside on your PC and facilitate faster, easier, multi-compound searching for metabolomics research.

The latest version of the METLIN PCD contains 679 compounds with retention times that enable more confident identification by using accurate-mass and retention-time (AMRT) matching. As a result of the continuing collaboration between Agilent Technologies and Dr. Gary Siuzdak, the METLIN PCDL contains accurate-mass Q-TOF MS/MS reference spectra for 2,278 compounds. Greater confidence in compound identification can be achieved by using MS/MS library spectral matching.



The METLIN Personal Compound Database (PCD) and the METLIN Personal Compound Database and Library (PCDL) facilitate faster, easier, multi-compound searching for metabolomics research.

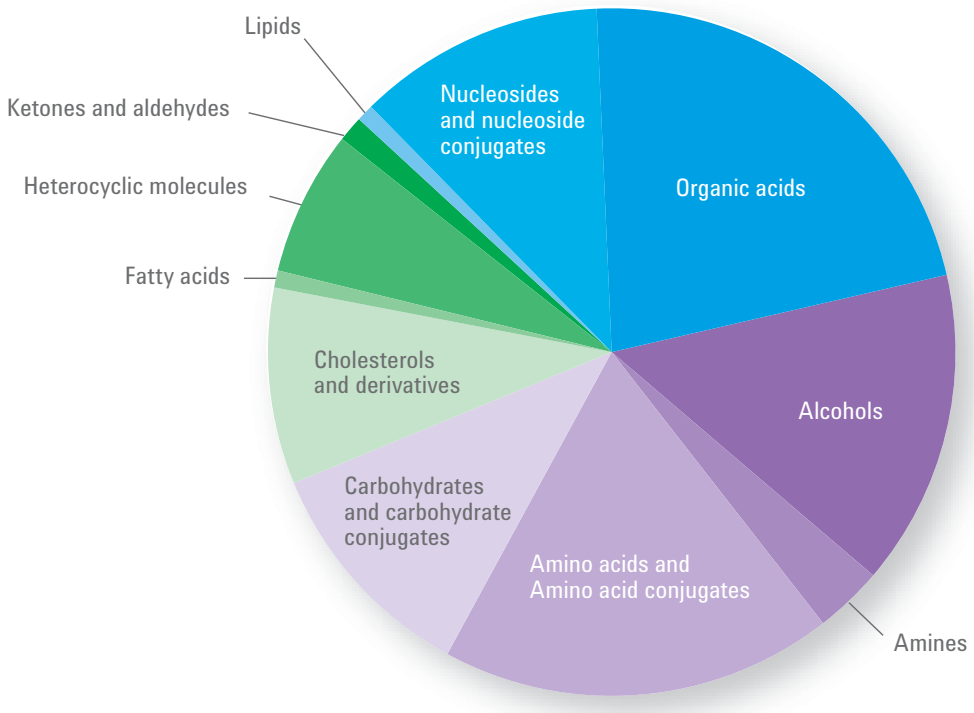
ACCURATE-MASS AND RETENTION-TIME MATCHING FOR HIGHER CONFIDENCE IDENTIFICATIONS

Accurate-mass matching is the most commonly used method to identify compounds in metabolomics research, but mass information alone is not enough to make a confident identification. Combining retention-time matching with accurate-mass matching results in greater confidence in compound identification.

The METLIN Metabolite PCD includes retention times for 679 standards that have been carefully determined using standardized chromatographic conditions. The standardization method used a simple linear-gradient, reverse-phase separation that applies to the majority of metabolites.

The reverse-phase method was designed for use with electrospray (ESI) and atmospheric chemical (APCI) ionization, as well as positive and negative mode ionization. Importantly, three different LC /MS systems and three different columns were used, and the extracted ion chromatogram of each standard was evaluated by a chemist, before the retention time was added to the METLIN PCD. The method was tested on a wide variety of sample matrices to verify applicability to many sample types.

To make it easy to find additional information, most compounds in the METLIN PCD are annotated with both a chemical formula and structure. Many entries also include CAS, HMDB, LMP, or KEGG identifiers as well as web links to the associated PubChem, Human Metabolome Database, Lipid Maps, and Kyoto Encyclopedia of Genes and Genomes database entries. You can also personalize the METLIN PCD by adding proprietary compounds, retention times, and MS/MS spectra. Create entries for metabolites labeled with stable isotopes as well, and add unmatched masses to the database for tracking across experiments.



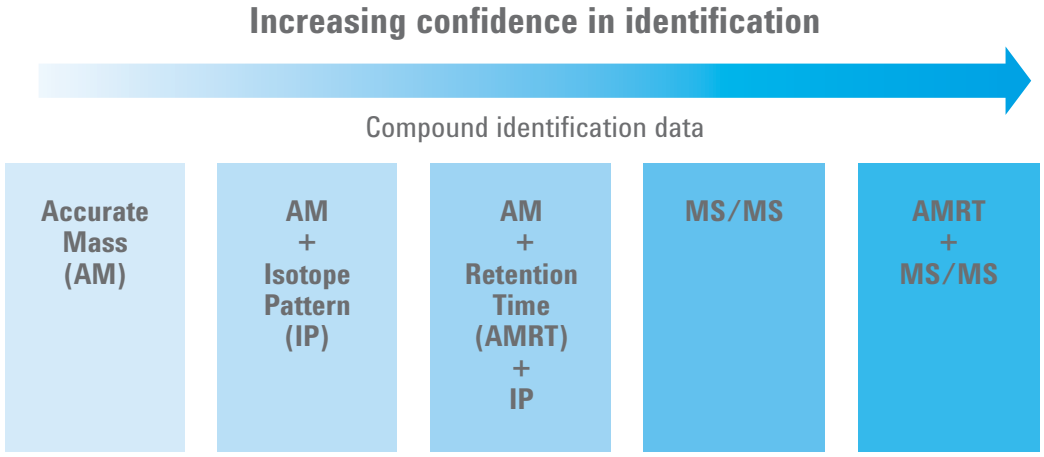
Distribution of superclass information for the METLIN PCD database using HMDB classification.

MS/MS MATCHING FOR THE HIGHEST CONFIDENCE IDENTIFICATIONS

While accurate-mass and retention-time matching alone can provide high-confidence identification of most compounds, adding MS/MS library searching capability provides a chromatography-independent means of compound identification. To provide you with the highest confidence in metabolite identification, MS/MS spectra have been added to 2,278 compounds in the METLIN Metabolite PCD to produce the METLIN Metabolite Personal Compound Database and Library (PCDL), which adds accurate-mass MS/MS library searching as a means of identifying metabolites. Matching unknowns to the high-quality spectra in the METLIN PCDL provides a level of certainty in identification that is unmatched by using other publicly available databases.

For the METLIN PCDL, a comprehensive approach was used to produce an MS/MS spectral library capable of handling the challenges of metabolomics. The library entries were generated from standards using an ESI source on multiple Agilent Q-TOF LC/MS instruments, to ensure reproducibility. In addition, since most metabolites ionize in only one mode, or poorly in one polarity and strongly in the other, spectra were collected in both positive and negative ion modes. Some compounds fragment easily, while others require more fragmentation energy to generate enough fragment ions to confirm identity, so spectra were also collected at three collision energies of 10, 20, and 40 eV.

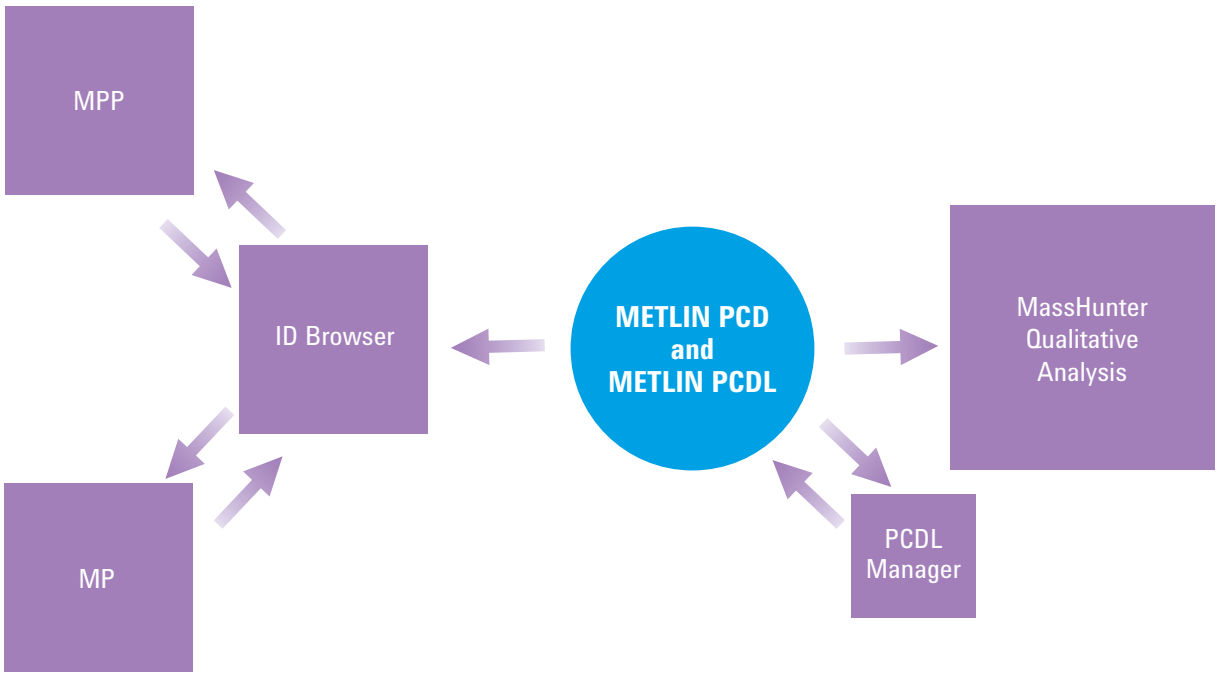
All spectra in the METLIN PCDL were subjected to rigorous quality control to produce a library containing only spectra of sufficient quality to be useful and provide accurate metabolite identification. Each observed fragment ion was tested using custom software to determine its assignment to a compound's MS/MS library spectrum, and was mass-corrected to its theoretical mass before adding to the spectrum. Then the original MS/MS spectrum was searched against the library to ensure that it matched the expected metabolite. Finally, the search results were reviewed by a chemist to remove any bad MS/MS spectra from the library.



The addition of orthogonal information increases confidence in compound identification.

SOFTWARE TOOLS HARNESS THE ADVANCED FEATURES OF METLIN METABOLITE PCD AND PCDL

Metabolite database information is only valuable if it can be efficiently utilized to produce high-confidence identifications. Agilent software tools facilitate your metabolomics compound identification, with an ease unmatched by other software tools. METLIN Metabolite PCD and PCDL content seamlessly integrate with Agilent LC/MS software tools for fast and easy compound matching in single and batch mode, with compound-centric data viewing to speed your identification review. An efficient database management tool enables you to edit your personalized database and library to reflect the work done in your laboratory. Trigger informational searches of web-based databases by simply clicking on the hyperlink associated with the KEGG, CAS, HMDB, LMP, or METLIN number returned as part of the database search.

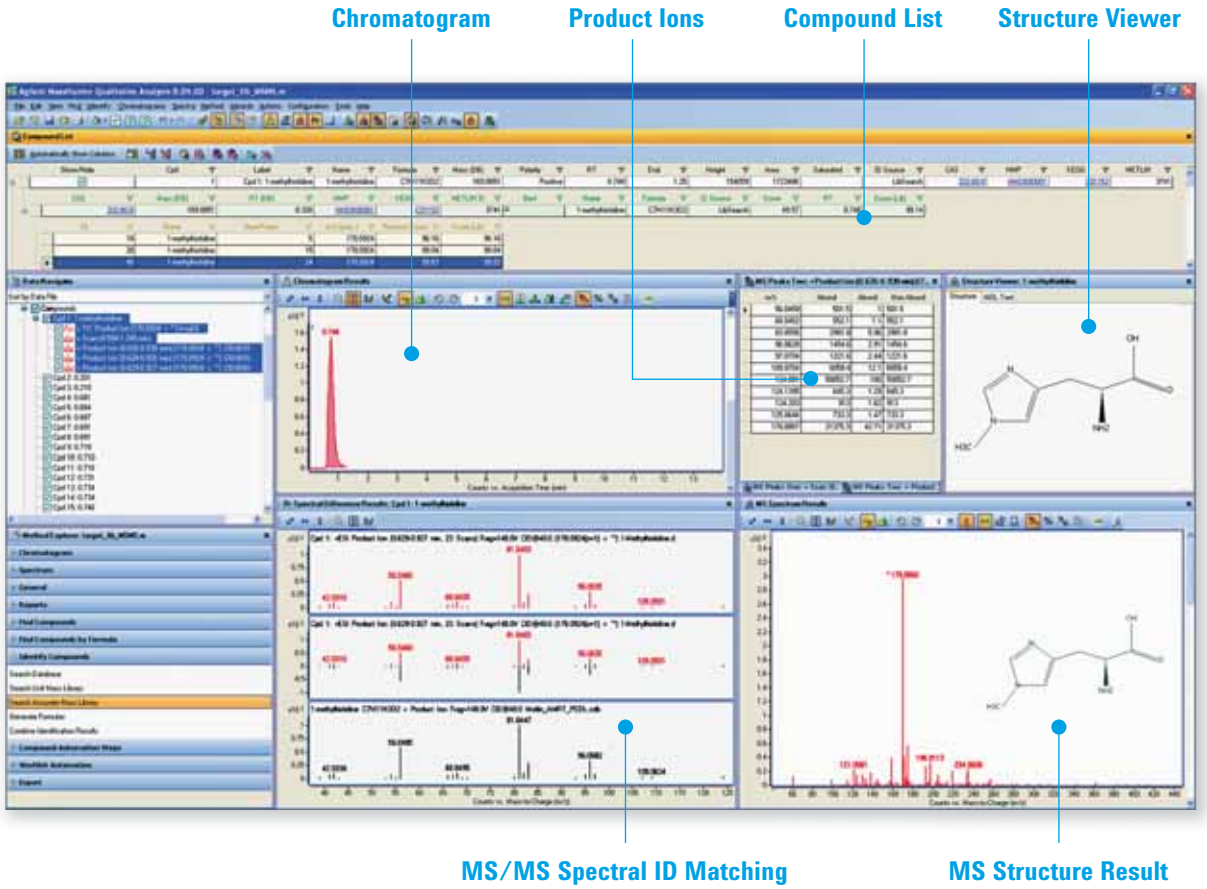


Software tools harness the advanced features of METLIN PCD AND PCDL.
METLIN PCD and PCDL content seamlessly integrate with Agilent LC/MS software tools for fast and easy compound matching.
MPP: Mass Profiler Professional software. MP: Mass Profiler software. Arrows indicate content flow.

A SELECTION OF DEDICATED MANAGEMENT AND SEARCH CAPABILITIES

MassHunter Qualitative Analysis

MassHunter Qualitative Analysis, a component of the popular MassHunter Workstation software suite, is the primary tool for analyzing untargeted metabolomics data. MassHunter Qualitative Analysis is used to extract compounds and MS/MS spectral information. Compound results are then searched using accurate-mass, retention-time, isotope-pattern, and MS/MS data to generate the highest-confidence metabolite identifications. Automatically perform multiple-compound searches simultaneously, or manually analyze a single spectrum or compound. Searches that utilize the PCD database or the PCDL MS/MS library even annotate the spectra with structures of the identified compounds. With its ease-of-use and compound-centric data viewing to speed your review, MassHunter Qualitative Analysis is the tool of choice for MS/MS identification.



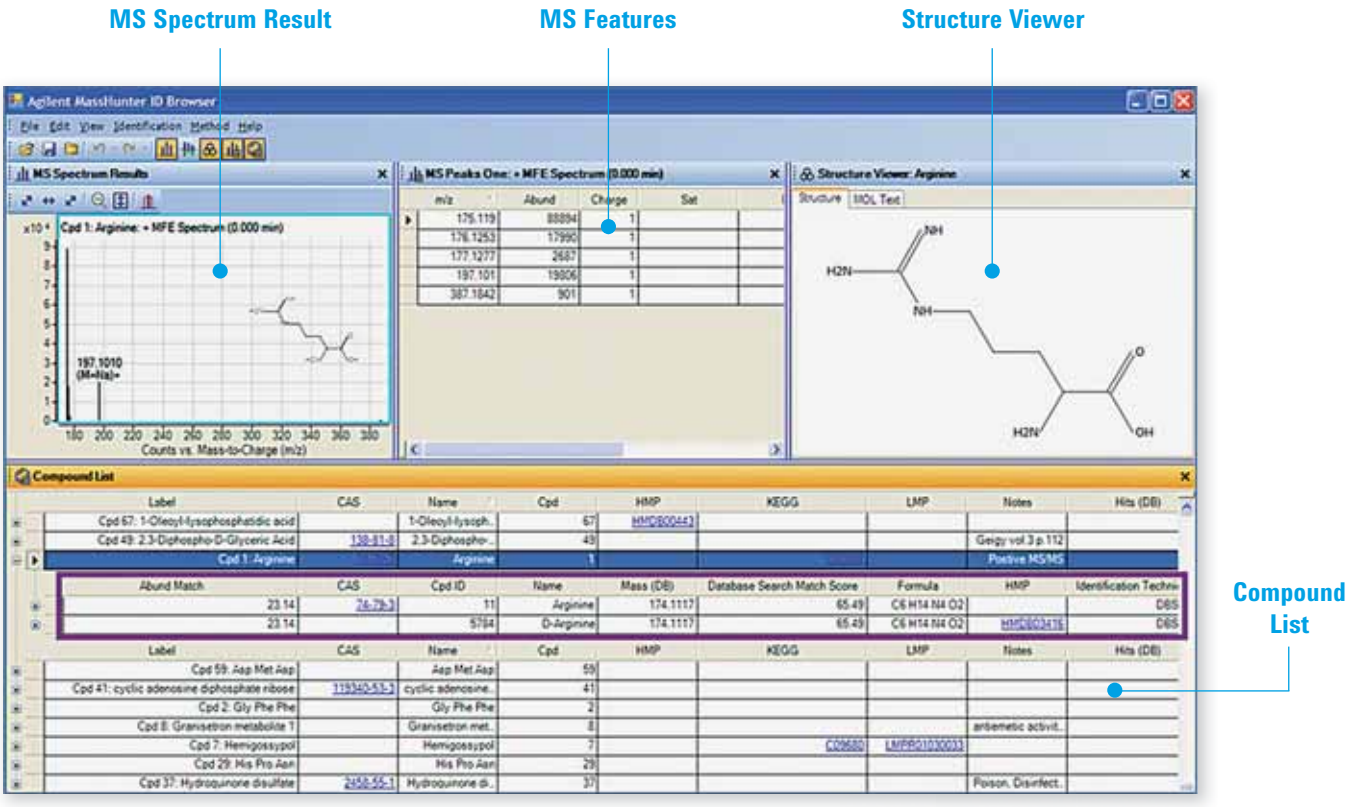
MassHunter Qualitative Analysis, a component of the popular MassHunter Workstation software suite, uses accurate-mass, retention-time, isotope-pattern, and MS/MS data to generate the highest-confidence, metabolite identifications.

ID Browser

ID Browser is a component of the widely used Agilent Mass Profiler (MP) and Mass Profiler Professional (MPP) software packages. It is used to generate compound identifications using accurate-mass, retention-time, and isotope-pattern matching, in both single- and batch-search modes, for fast and productive metabolomics research. With ID Browser, the best database match is listed for each submitted mass, and you can review other possibilities and override the search result as necessary. ID Browser then automatically annotates the retention time and mass entries in MP and MPP software to include the search results.

PCDL Manager

PCDL Manager lets you curate and modify the METLIN Metabolite PCD and PCDL to meet your research needs. The combination of the METLIN PCD or PCDL with PCDL Manager gives you complete control of your database content and ensures the security of your work by keeping your intellectual property on site. You can personalize your METLIN PCD or PCDL by adding proprietary compounds, retention times, and MS/MS spectra. PCDL Manager also provides limited searching capability for compounds in both PCDs and PCDLs using text, formula, accurate mass, and retention time. You can search, browse, or clean up MS/MS spectra in PCDLs, and link to websites to obtain more information on compounds.



ID Browser generates compound identifications using accurate-mass, retention-time, and isotope-pattern matching, in both single- and batch-search modes, for fast and productive metabolomics research.

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