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COMPUTER SOFTWARE
REVIEWS

ACD/Method Development Software Suite, Version 6.0. Advanced Chemistry Development, 600-90 Adelaide Street West, Toronto, Ontario M5H 3V9, Canada. www.acdlabs.com. Contact Company for Pricing Information.

The use of computer calculations to develop analytical methods has achieved broad popularity due to the dramatic increase in the calculating power of the PC and our understanding of relationships between chemical structures and their physicochemical behavior. The software that is the subject of this review is aimed at combining searchable database management with the ability to predict and optimize chromatographic behavior of substances of interest.

The installation of the software on a computer equipped with a 1.8 GHz CPU and 512 MB of memory using the Windows XP system was very simple and straightforward, including an online update. Because the updated files of the entire suite exceed 200 MB in size, their installation requires a wideband Internet connection.

The expandable software suite for evaluation includes eight subprograms: Chemsketch, 3D Viewer, HNMR Viewer, CNMR Viewer, SpecManager, Spectrum Database, GC Simulator, and LC Simulator. Other useful tools and plug-ins, such as NMR predictor and MS manager, can be purchased and integrated into the suite. Two programs in the software, HNMR viewer and CNMR viewer, were not reviewed because no sample files were provided.

The software is reasonably well organized, and switching between each program is easy, although not seamless. Chemical information is linked with the Spectrum Database, which can be accessed by searching by name or by structure. However, the programs sometimes jump from one window to another or even disappear for no obvious reason. Although the software is touted for its integration of the various programs, there is no road map to assist the user in understanding how the different programs and windows work together. On the other hand, a very welcome feature of the software is its facility for simultaneously recalling the chemical structure and chromatogram of a substance.

One of the key programs within the suite is Chemsketch, which is not only a powerful chemical drawing package, but also serves as an entry to database searching and a bridge to programs for predicting chromatographic properties. Chemsketch includes all of the basic drawing functions that are offered by other popular chemical drawing softwares, for example, Chemdraw, ISIS/Draw, and Chemwindow. In addition, Chemsketch allows for the import and export of files to the above-mentioned drawing programs, making it fully compatible with them. The files can also be easily converted to PDF and html formats, which helps when transferring data into Web-based programs. One of the features we particularly liked about Chemsketch was the optimization of 3D structures that automatically generated optimized conformations. This feature allowed the user to rotate the structure easily by moving the cursor and to copy it into 3D viewer to obtain colorful 3D drawings. Furthermore, certain parameters, for example, bond angles and atomic distances, could be measured directly from the structure. Another nice feature allowed the user to generate the name of the structure by simply clicking a button. Unfortunately, the software that we evaluated could not handle more than 50 atoms or 3 rings, and some functions in the program required additional payment and registration.

This version had no function that allowed generation of a structure from the name of the chemical; this feature would be very useful to chemists by eliminating the tediousness of drawing chemical structures. We also found that the function "replace element" did not correctly replace elements in the formula. The user can report bugs such as this by going to the help menu, and new features may be requested via the Web by this means as well.

Unfortunately, the help files were not very helpful, although the software did include several guides in Microsoft Word format. These were more like the manuals traditionally provided by the manufacturer. The program also had a large collection of structures of more complex but commonly used compounds, which included alkaloids, DNA/RNA, carbohydrates, etc. It also contained a built-in dictionary of ca. 100 000 compounds categorized according to their therapeutic effects. The physicochemical properties of those compounds, for example, density and surface tension, were included or could be calculated by the program.

SpecManager is the management tool of the Spectrum database, which is compatible with most HPLC, CE, and GC data generated by instruments from various manufacturers and includes all of the basic data-handling functions. Some of them, for example, peak deconvolution, may be helpful for quantification when they are not included in the software bundled with the operating instrument. In addition, SpecManager unifies the format for the data, making it easy to search and manage. One of the obvious advantages of this tool is the ability to search by the chemical structure to find the chromatogram/spectrum in the database. Although this technology has been used in other search engines, such as SciFinder, the distinguishing feature of this program is its ability to link the chemical structure with its chromatographic behavior. It makes the software potentially more powerful than either a purely chromatographic software or a search-based software alone and therefore facilitates method development and saves time. Unfortunately, a large and open database is required for collecting useful information not only from the manufacturer but also from the literature. The database in this software relies mainly on information provided by the LC/GC column suppliers and, therefore, may miss valuable information from the scientific literature.

Reliable methods for high-resolution separations are traditionally developed by trial and error. To optimize a separation is always time-consuming and requires some luck, particularly in

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selecting the right column. The development of computer-assisted methods has been a major step forward in addressing this issue, and numerous simulation programs are now available. For example, Dry-lab has been commercially available for over 15 years for HPLC. Most of these programs are based on the quantitative structure retention relationship in chromatography, a research topic for some 50 years and one that remains of intense interest. The migratory behavior of the sample components can be predicted by following the rules in the selection of the right stationary and mobile phases. This is especially true for small neutral compounds in reversed phase chromatography and for small charged sample components in ion-exchange chromatography. Many drug substances fall into this category, and appropriate software can be helpful for optimizing their separation.

One of the distinctive features of the LC Simulator in the present program is that it not only predicts optimal conditions for separations by calculating the experimental data of several HPLC runs, but also tries to predict the chromatogram on the basis of the chemical structure. The number of the runs is dependent on how many parameters need to be optimized, for example, the gradient profile, pH, and temperature. There are two ways to do that using this program. One is by direct calculation from log *P*, where *P* is the 1-octanol−water partition coefficient. We selected vitamin B_2, a molecule with three rings and four OH groups, as a test for this approach. The calculation failed on our computer. This suggests that the program is unable to deal with more complex structures. In addition, even though log *P* was achieved, the simulated chromatogram was still very crude because of the many factors involved in the separation. An alternate method recommended for predicting a chromatogram on the basis of the chemical structure is to search for the substance in the database to see whether a chromatogram is available for the compound. Given the limited database, it is difficult to get a perfect match.

Alternatively, it is possible to search for a fragment of the chemical structure to get an estimate of the separation for structurally related compounds and then further predict the chromatogram of the substance by considering the contributions of structural changes. The prediction by using this method, however, is expected to be less accurate, especially when predicting the separation of a mixture having widely different chromatographic properties from those achieved from the database search. Because the chromatograms extracted from the database are column-dependent, the prediction will also be dependent on the column selected. In practice, it is hard to find a column that matches the user's column. Furthermore, we searched the ISI Web of Science database and found no peer-reviewed publications using this software to optimize LC separations nor could we find any from the company's Web site. On the other hand, we found more than 10 papers using Dry-lab, another LC simulation software. Comparison is rather difficult, however, because this software may be so new that it has not yet appeared in the recent literature.

In our view, the stability of the software needs to be strengthened, especially when switching between different programs. The help file is the weakest part, because some files are misplaced, and some of them are simply missing. The software should be very useful in R & D laboratories when these drawbacks are overcome and the database is expanded to improve chromatographic predictions. Because ACD Labs provides a fairly large choice of scientific tools to cover most types of spectroscopy and chromatography, it is easy to upgrade or expand the software to manage different types of data, once the user is familiar with the software.

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