MSforID: a robust and transferable tandem mass spectral library

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Abstract

MSforID represents a library of tandem mass spectra obtained from (quasi-)molecular ions produced by atmospheric pressure ionization methods. At the current stage of development the library contains 12,122 spectra of 1,208 small (bio-)organic molecules. For library search a tailor-made search algorithm is available which exhibits a high tolerance towards changes within the intensity distribution among different fragmentation pathways. With a set of more than 5,000 spectra independently acquired on different kinds of instruments, performance of the library was tested. The obtained results revealed that the MSforID library represents a reliable, robust and universal tool for the identification of small bioorganic molecules that is ready-to-use in different fields of application such as forensics, metabolomics, pharmaceutical research, toxicology, and environmental analysis.

1. Introduction

Mass spectral libraries play an important role in qualitative analysis for the identification of unknown compounds. The development of tandem mass spectral libraries began in the late 1990s triggered by the invention of atmospheric pressure ionization techniques. It was soon realized that collision induced decomposition is difficult to control. The limited reproducibility of tandem mass spectra was found to represent a major obstacle for the development of robust and transferable libraries. To overcome these limitations, we have developed a new concept for the setup of tandem mass spectrometric libraries. These efforts have led to the development of the MSforID library.

2. Material and Methods

The MSforID project (www.msforid.com) relies on the combination of a highly efficient search algorithm with a comprehensive mass spectral library established on a high-resolution mass spectrometer [1-3]. The tailor-made search algorithm is based on peak matching and exhibits a high tolerance towards changes within the intensity distribution among different fragmentation pathways. The reference library was established on a quadrupole−quadrupole−time-of-flight instrument (QqTOF) using ten different collision energies for acquiring compound-specific reference spectra. At the current stage of development the library contains 12,122 spectra corresponding to 1,208 reference compounds. With a set of more than 5,000 spectra independently acquired on different kinds of instruments, reliability of search results and transferability of the library were tested.

3. Results and Discussion

Different experiments were conducted to evaluate the performance of the MSforID library. In a first set of experiments, individual spectra of the MSforID library were searched against the

whole library after excluding either this single compound-specific spectrum or all compound-specific spectra prior to searching [4]. The percentage of correct positive results (= sensitivity) was 99.3%. The percentage of correct negative results (= specificity) was 92.9%.

Next, the Weinmann library was used as test set to evaluate the performance of the MSforID library. The Weinmann library contained over 5,600 spectra of 1253 compounds acquired on a quadrupole−quadrupole−linear ion trap (QqLIT) instrument. The spectra acquired in positive ion mode (4368) were used for the evaluation of the library search performance. A sensitivity of 97.4% and a specificity of 92.3% were obtained.

In a final set of experiments, 1242 spectra of 20 compounds acquired by several operators on different instruments located in multiple laboratories was used as sample set. Although a plurality of experimental setups was used to generate tandem mass spectrometric data, sensitivity exceeded 95%, which clearly proves that the MSforID library is robust and transferable.

Tab. 1. Results of three experiments to evaluate the performance of the MSforID library.

Data set		**Spectra**	**Sensitivity [%]**	**Specificity [%]**
Experiment 1	MSforID	10,712	99.3	92.9
Experiment 2	Weinmann library	4,368	97.4	92.3
Experiment 3	QqQ	63	98.4	
	IT	228	100	
	LIT I	63	98.4	
	LIT II	240	95.4	
	QqLIT - pi	63	98.4	
	QqLIT - epi	78	97.4	
	QTOF I	63	98.4	
	QTOF II	141	95.0	
	Orbitrap	240	99.3	
	LIT-FT	63	100	

The MSforID library is a reliable, robust and universal tool for the identification of small bio-organic molecules. Fields of application include forensics, metabolomics, pharmaceutical research, toxicology, environmental analysis.

In forensic toxicology the library is particularly useful for:

(1) Systematic toxicological analysis (STA): Since the outcome of STA can have pivotal judicial, social, personal and/or economic consequences, a number of analytical procedures should be used to minimize the probability of false results. In this context, LC/MS(/MS) under data-dependent acquisition control with automated library search can complement existing screening approaches.
(2) Identification of illicit and counterfeit drugs [1,5]: Fast and efficient identification of potentially toxic compounds present within illicit and counterfeit drugs can be accomplished via automated matching of corresponding tandem mass spectra.
(3) Development of quantitative methods [6]: Single and multiple reaction monitoring are integral parts of quantitative LC/MS/MS approaches. The library is very useful to choose appropriate precursor-to-product ion transitions. Furthermore, the selectivity of transitions can easily be checked via search within the library.
(4) Metabolite profiling [7]: Library search can be used to verify the structural relatedness of putative metabolites to the precursor drug.

4. Conclusion

The MSforID library is a reliable tool for the identification of small molecules. Specificity is usually higher than >95%; sensitivity exceeds 92%. The MSforID library shows a very good transferability to a huge variety of tandem mass spectrometric instruments. Possible fields of applications include forensics, metabolomics, pharmaceutical research, toxicology, and environmental analysis.

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6. References

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