

High throughput accurate mass measurement using the LDTD ion source on the LTQ Orbitrap

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OVERVIEW

Purpose – Evaluate the performance of the LDTD ion source in positive ion mode on the LTQ Orbitrap mass spectrometer for accurate mass measurements (AMMs) of small molecules.

Methods – Analysis of 150 natural and synthetic compounds using ESI, APCI and LDTD in positive ion mode.

Results – LDTD provides better performances than ESI and APCI in terms of throughput, ease of use, spectral quality and specificity for polyaromatic biomolecule detection. In terms of sensitivity and success rate for AMMs, LDTD is comparable to ESI and APCI. Overall results show that the LDTD ion source mounted on the LTQ Orbitrap is ideally suited for AMMs of small molecules within a MS core facility.

INTRODUCTION

Accurate mass measurements (AMMs) of small molecules by mass spectrometry were mostly performed on magnetic sector instruments until the end of the last century. Although these instruments provide sufficient accuracy/resolution for AMMs, they suffer from important limitations compared to new generations of high-resolution instruments. Sector instruments are difficult to use and to operate, their throughput is low and reference compounds are scarce. The complexity of spectra, ESI/APCI sources have revolutionized the analysis of small molecules by LDTD and for MS/MS. Nevertheless, these analyses present their own drawbacks like throughput limited to less than 30 samples/hour, high solvent consumption, requirement of an autosampler and LC platform.

The present work involves the coupling of two new technologies for performing very high throughput AMMs. The LDTD (Laser Doped Thermal Desorption) source (Phytionix Technologies) has been mounted on the LTQ Orbitrap mass spectrometer (ThermoFisher Scientific). The LDTD technology consists of a rapid desorption of a small sample followed by atmospheric pressure chemical ionization without solvent. The thermal desorption is produced by an infrared laser beam focused at the back of each sample on a highly reflective well plate. The LTQ Orbitrap is a novel instrument combining all the features of the LTQ linear ion trap with those of the Orbitrap. It offers the best mass resolution, high mass accuracy (~5 ppm, external calibration), and high resolving power (up to 500,000). All analyses were performed on the LTQ Orbitrap.

The potential of the LDTD ion source for AMMs of organic molecules is demonstrated using hundreds of natural and synthetic compounds.

Table 1 – Relative intensity (RI) of various molecules analysed with ESI, APCI and LDTD ion sources

Sample	ESI	APCI	LDTD
101	100	100	100
102	100	100	100
103	100	100	100
104	100	100	100
105	100	100	100
106	100	100	100
107	100	100	100
108	100	100	100
109	100	100	100
110	100	100	100
111	100	100	100
112	100	100	100
113	100	100	100
114	100	100	100
115	100	100	100
116	100	100	100
117	100	100	100
118	100	100	100
119	100	100	100
120	100	100	100
121	100	100	100
122	100	100	100
123	100	100	100
124	100	100	100

Sample	ESI	APCI	LDTD
125	100	100	100
126	100	100	100
127	100	100	100
128	100	100	100
129	100	100	100
130	100	100	100
131	100	100	100
132	100	100	100
133	100	100	100
134	100	100	100
135	100	100	100
136	100	100	100
137	100	100	100
138	100	100	100
139	100	100	100
140	100	100	100
141	100	100	100
142	100	100	100
143	100	100	100
144	100	100	100
145	100	100	100
146	100	100	100
147	100	100	100
148	100	100	100
149	100	100	100
150	100	100	100

Sample	ESI	APCI	LDTD
151	100	100	100
152	100	100	100
153	100	100	100
154	100	100	100
155	100	100	100
156	100	100	100
157	100	100	100
158	100	100	100
159	100	100	100
160	100	100	100
161	100	100	100
162	100	100	100
163	100	100	100
164	100	100	100
165	100	100	100
166	100	100	100
167	100	100	100
168	100	100	100
169	100	100	100
170	100	100	100
171	100	100	100
172	100	100	100
173	100	100	100
174	100	100	100
175	100	100	100
176	100	100	100
177	100	100	100
178	100	100	100
179	100	100	100
180	100	100	100

Sample	ESI	APCI	LDTD
181	100	100	100
182	100	100	100
183	100	100	100
184	100	100	100
185	100	100	100
186	100	100	100
187	100	100	100
188	100	100	100
189	100	100	100
190	100	100	100
191	100	100	100
192	100	100	100
193	100	100	100
194	100	100	100
195	100	100	100
196	100	100	100
197	100	100	100
198	100	100	100
199	100	100	100
200	100	100	100
201	100	100	100
202	100	100	100
203	100	100	100
204	100	100	100
205	100	100	100
206	100	100	100
207	100	100	100
208	100	100	100
209	100	100	100
210	100	100	100
211	100	100	100
212	100	100	100
213	100	100	100
214	100	100	100
215	100	100	100
216	100	100	100
217	100	100	100
218	100	100	100
219	100	100	100
220	100	100	100
221	100	100	100
222	100	100	100
223	100	100	100
224	100	100	100
225	100	100	100
226	100	100	100
227	100	100	100
228	100	100	100
229	100	100	100
230	100	100	100
231	100	100	100
232	100	100	100
233	100	100	100
234	100	100	100
235	100	100	100
236	100	100	100
237	100	100	100
238	100	100	100
239	100	100	100
240	100	100	100

Table 2 – Efficiency of ESI, APCI and LDTD for accurate mass measurements (AMMs) of small molecules.

	ESI	APCI	LDTD
Number of samples	150	150	150
Number of identification	142	139	141
Specificity of each molecule	81.4%	85.4%	94.0%
Success rate for AMM	95%	85%	98%

Table 3 – Molecules for which no molecular ion of significant relative intensity were detected with LDTD

Sample	ESI	APCI	LDTD
181	100	100	100
182	100	100	100
183	100	100	100
184	100	100	100
185	100	100	100
186	100	100	100
187	100	100	100
188	100	100	100
189	100	100	100
190	100	100	100
191	100	100	100
192	100	100	100
193	100	100	100
194	100	100	100
195	100	100	100
196	100	100	100
197	100	100	100
198	100	100	100
199	100	100	100
200	100	100	100
201	100	100	100
202	100	100	100
203	100	100	100
204	100	100	100
205	100	100	100
206	100	100	100
207	100	100	100
208	100	100	100
209	100	100	100
210	100	100	100
211	100	100	100
212	100	100	100
213	100	100	100
214	100	100	100
215	100	100	100
216	100	100	100
217	100	100	100
218	100	100	100
219	100	100	100
220	100	100	100
221	100	100	100
222	100	100	100
223	100	100	100
224	100	100	100
225	100	100	100
226	100	100	100
227	100	100	100
228	100	100	100
229	100	100	100
230	100	100	100
231	100	100	100
232	100	100	100
233	100	100	100
234	100	100	100
235	100	100	100
236	100	100	100
237	100	100	100
238	100	100	100
239	100	100	100
240	100	100	100

DISCUSSION

The LTQ Orbitrap is ideally suited for accurate mass measurements using the LDTD ion source because mass accuracy lower than 3 ppm is obtained with this calibration. This is similar to what is obtained with the sample for AMMs. The mass error range varied from 0.1 to 3 ppm for all analysis and was not affected by the ion source used on the LTQ Orbitrap. In terms of spectral quality, the LDTD spectra are cleaner than ESI and APCI spectra for most compounds (see Figure 3). Overall, the success rate of the LDTD source for detecting small molecules is comparable to ESI and slightly better than APCI (see Tables 1 and 2). Moreover, the LDTD source shows a unique specificity for the analysis of polyaromatic compounds over ESI and APCI (see Figure 2) and other classes of molecules (see Table 3). The only limitation of the LDTD source, observed so far, is its poor efficiency for the analysis of thermolabile biomolecules such as proteins and low mass of small molecules (see Table 3). Thermal fragmentation must occur before vaporization of the labile biomolecules, the sampling rate obtained with the LDTD source on the LTQ Orbitrap is approximately 300 samples per hour (Figure 4) while the best reachable rate with ESI and APCI is less than 30 samples per hour.

CONCLUSIONS

- Strengths of the LDTD source**
- Highest throughput for accurate mass measurements (300 samples/hour)
 - Success rate for AMMs comparable to ESI and better than APCI
 - LDTD provides better spectral quality than ESI and APCI for most compounds
 - Specificity for the analysis of polyaromatics and other classes of molecules containing few functional groups
- Limitation**
- Poor efficiency for the analysis of thermolabile biomolecules such as peptides

The coupling of the LDTD ion source with LTQ Orbitrap hybrid mass spectrometer is the ideal solution for high throughput AMMs of small molecules.

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METHODS

Figure 1 – The LDTD ion source

Sample plate: SOLID
Thermal desorption: induced inductively by laser at 980 nm (infrared)
Sample: ionized by the carrier gas
Ionization: carried out by a corona discharge (constant voltage)

Instrumental parameters:
 All ion sources were operated in positive ion mode without any method development for each sample. Standard parameters were used for all three sources. The laser power energy of the LDTD source was set to 18.0 mJ/cm².

Mobile phase and flow rate:
 ESI: 60MMAH – 0.1%FA, flow rate: 20 µL/min (ThermoFisher)
 APCI: 60MMAH – 0.1%FA, flow rate: 300 µL/min (ThermoFisher)
 LDTD: no mobile phase, carrier gas: N2 (99.999%) (Phytionix)
 Mass spectrometer: LTQ Orbitrap (operated at RP-30,000) (ThermoFisher)

