Assessment of paper tip angular position, carryover, matrix effects and dried blood spot storage effect on paper spray mass spectrometry

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**Supplemental Figure 1**: The paper spray prototype interfaced to MS inlet. (Left) Closed with plastic case to prevent excessive drying of samples due to the air and as a safety shield (Right) opened to display the paper substrate fixed to the clipper and the paper tip positioned at an angle towards the MS inlet. Positioned on top of the paper substrate (Right) is the silica capillary (100 µm ID) which apply the solvent continuously onto the paper substrate using the programmed LC method.
Supplemental Figure 2: Sequential solvent application program. The delivery of the spray solvent initiates with a flow rate of 200 µL/min from 0.002 min to 0.095 min (A) and reduced to 15 µL/min from 0.096 to 1 min (B). A total spray volume of about 32 µL was delivered onto the paper substrate.
Supplemental Figure 3. Absolute signal responses of test compounds in matrix-based papers. For sunitinib, the signal response from Grade ET 31 was significantly different from the rest of the papers, except filter paper. Filter paper obtained the highest signal response for imatinib, which was significantly different from the rest of the papers. The signal response for benzethonium from silica coated paper was significantly different from the other papers. Grade 1 Chr paper’s signal response for dasatinib was significantly different from other papers, except filter paper, whilst nilotinib obtained the highest signal response from filter paper which was significantly different from the papers except Grade ET 31. Significance difference (*) (p ≤ 0.05).
**Supplemental Table 1:** General information on the physical properties of the papers from manufacturer (Whatman) website.

<table>
<thead>
<tr>
<th>Paper type</th>
<th>Thickness (mm)</th>
<th>Flow rate (mm/30min)</th>
<th>Pore size (µm)</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>SG 81 ion exchange paper</td>
<td>0.27</td>
<td>110</td>
<td>-</td>
<td>Surface of cellulose coated with silica</td>
</tr>
<tr>
<td>Grade ET31Chr</td>
<td>0.50</td>
<td>225</td>
<td>21.5</td>
<td>Thick chromatography paper with the highest flow rate</td>
</tr>
<tr>
<td>Grade 1 Chr</td>
<td>0.18</td>
<td>130</td>
<td>11</td>
<td>Smooth surface chromatography paper</td>
</tr>
<tr>
<td>Grade 1 qualitative filter paper</td>
<td>0.18</td>
<td>-</td>
<td>-</td>
<td>Standard grade filter paper, 125 mm, circles</td>
</tr>
</tbody>
</table>

**Supplemental Table 2:** Tandem mass spectrometry setting for selected reaction monitoring for PS-MS/MS.

<table>
<thead>
<tr>
<th>Compound name</th>
<th>Parent ion (m/z)</th>
<th>Fragment ion (m/z)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>494</td>
<td>394</td>
</tr>
<tr>
<td>benzethonium</td>
<td>412</td>
<td>320</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>488</td>
<td>401</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>530</td>
<td>289</td>
</tr>
<tr>
<td>Sunitinib</td>
<td>399</td>
<td>326</td>
</tr>
<tr>
<td>Sunitinib-d10</td>
<td>409</td>
<td>326</td>
</tr>
</tbody>
</table>
**Supplemental Table 3:** The absolute matrix effect in paper spray mass spectrometry. The MS/MS signal responses (AUC) of test compounds in neat and blood matrices obtained from the analyses of four different paper substrates.

<table>
<thead>
<tr>
<th></th>
<th>Neat matrix</th>
<th>Blood matrix</th>
<th>Analyte signal in blood relative to Neat matrix</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Qualitative filter paper</td>
<td>Grade 1 Chr</td>
<td>Silica coated</td>
</tr>
<tr>
<td>Sunitinib</td>
<td>7.52E+06</td>
<td>7.58E+06</td>
<td>1.75E+06</td>
</tr>
<tr>
<td>Imatinib</td>
<td>8.68E+05</td>
<td>4.18E+05</td>
<td>1.05E+05</td>
</tr>
<tr>
<td>Benzethonium</td>
<td>1.95E+06</td>
<td>7.13E+05</td>
<td>9.46E+05</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>4.49E+05</td>
<td>4.70E+05</td>
<td>1.51E+05</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>7.37E+05</td>
<td>1.24E+06</td>
<td>2.14E+05</td>
</tr>
<tr>
<td></td>
<td>Qualitative filter paper</td>
<td>Grade 1 Chr</td>
<td>Silica coated</td>
</tr>
<tr>
<td>Sunitinib</td>
<td>1.88E+05</td>
<td>1.26E+05</td>
<td>1.26E+05</td>
</tr>
<tr>
<td>Imatinib</td>
<td>7.74E+04</td>
<td>2.88E+04</td>
<td>2.18E+04</td>
</tr>
<tr>
<td>Benzethonium</td>
<td>8.74E+04</td>
<td>5.37E+04</td>
<td>1.57E+05</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>7.40E+03</td>
<td>8.02E+03</td>
<td>4.18E+03</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>2.85E+04</td>
<td>1.32E+04</td>
<td>6.81E+03</td>
</tr>
</tbody>
</table>

|                  | Qualitative filter paper         | Grade 1 Chr                      | Silica coated                                  | Grade ET31Chr |
| Sunitinib        | 0.02                             | 0.02                             | 0.07                                           | 0.04           |
| Imatinib         | 0.09                             | 0.07                             | 0.21                                           | 0.04           |
| Benzethonium     | 0.04                             | 0.08                             | 0.17                                           | 0.03           |
| Dasatinib        | 0.02                             | 0.02                             | 0.03                                           | 0.02           |
| Nilotinib        | 0.04                             | 0.01                             | 0.03                                           | 0.01           |

**Supplemental Table 4:** Physical properties of the test compounds obtained from drug bank.

<table>
<thead>
<tr>
<th>Test Compound</th>
<th>Molecular weight</th>
<th>LogP</th>
<th>pK_a (acid)</th>
<th>pK_a (base)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sunitinib</td>
<td>398.473</td>
<td>3.24</td>
<td>11.46</td>
<td>9.04</td>
</tr>
<tr>
<td>Imatinib</td>
<td>493.602</td>
<td>3.47</td>
<td>12.45</td>
<td>8.27</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>529.515</td>
<td>4.51</td>
<td>12.38</td>
<td>5.92</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>488.000</td>
<td>2.77</td>
<td>8.49</td>
<td>7.22</td>
</tr>
<tr>
<td>Benzethonium</td>
<td>412.637</td>
<td>3.13</td>
<td>17.31</td>
<td>-4.10</td>
</tr>
</tbody>
</table>