Electronic Supplementary Material (ESI) for Analytical Methods.

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

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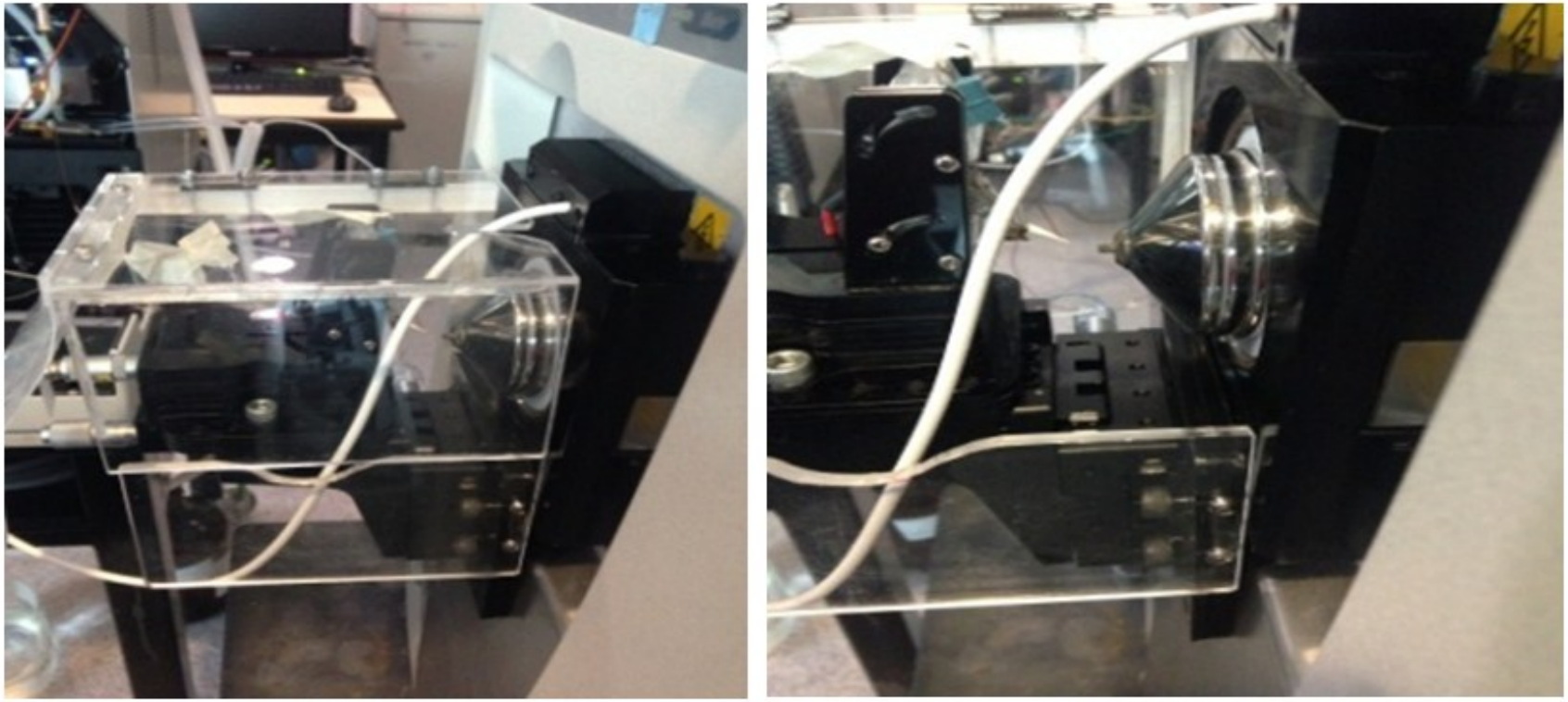
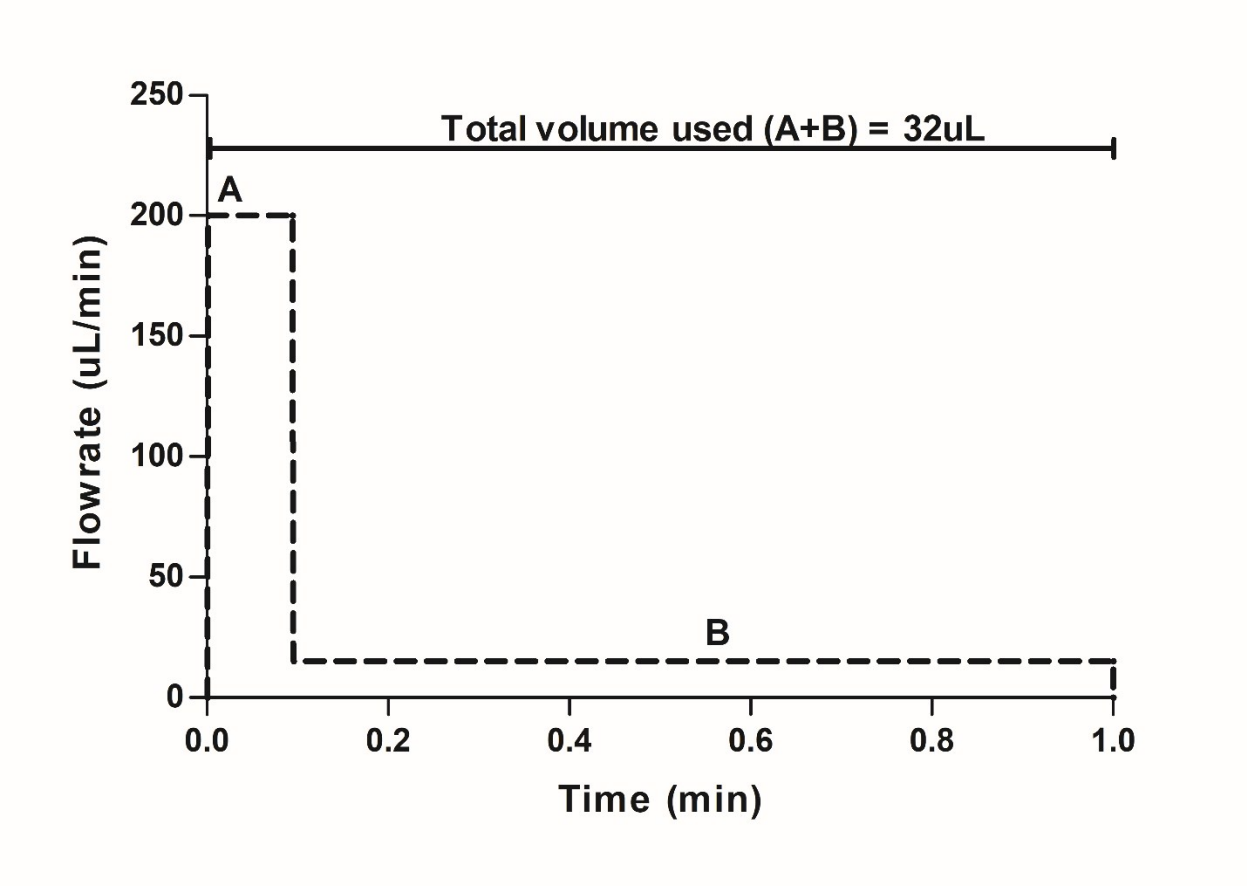
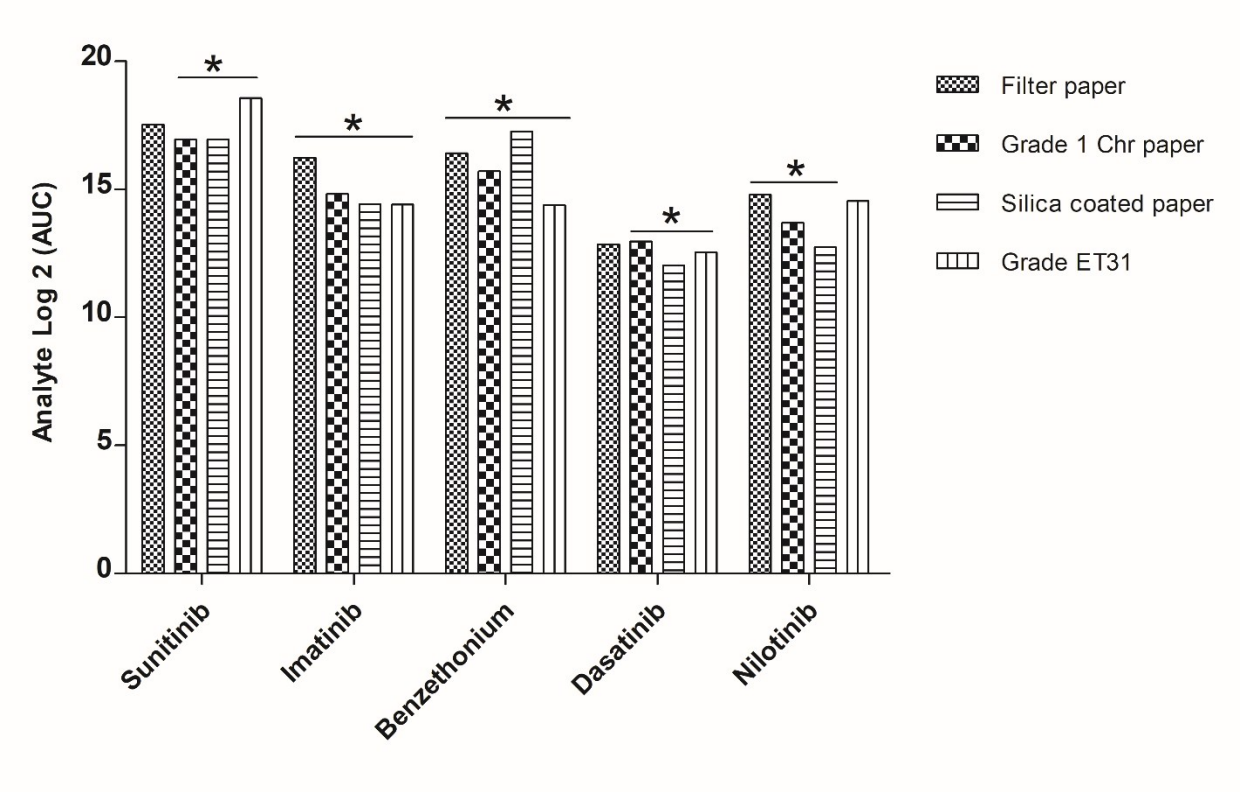


Supplemental Figure 1: The paper spray prototype interfaced to MS inlet. (Left) Closed with plastic case to prevent excessive drying of samples due to the air and as a safety shield (Right) opened to display the paper substrate fixed to the clipper and the paper tip positioned at an angle towards the 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 (*) ($p \leq 0.05$).

Supplemental Table 1: General information on the physical properties of the papers from manufacturer (Whatman) website.

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

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

Compound name	Parent ion (*m/z*)	Fragment ion (*m/z*)
Imatinib	494	394
benzethonium	412	320
Dasatinib	488	401
Nilotinib	530	289
Sunitinib	399	326
Sunitinib-d10	409	326

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.

Neat matrix

	Qualitative filter paper	Grade 1 Chr	Silica coated	Grade ET31Chr
Sunitinib	7.52E+06	7.58E+06	1.75E+06	1.04E+07
Imatinib	8.68E+05	4.18E+05	1.05E+05	5.51E+05
Benzethonium	1.95E+06	7.13E+05	9.46E+05	6.49E+05
Dasatinib	4.49E+05	4.70E+05	1.51E+05	3.95E+05
Nilotinib	7.37E+05	1.24E+06	2.14E+05	2.20E+06

Blood matrix

	Qualitative filter paper	Grade 1 Chr	Silica coated	Grade ET31Chr
Sunitinib	1.88E+05	1.26E+05	1.26E+05	3.89E+05
Imatinib	7.74E+04	2.88E+04	2.18E+04	2.16E+04
Benzethonium	8.74E+04	5.37E+04	1.57E+05	2.13E+04
Dasatinib	7.40E+03	8.02E+03	4.18E+03	5.97E+03
Nilotinib	2.85E+04	1.32E+04	6.81E+03	2.38E+04

Analyte signal in blood relative to Neat matrix

	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.

Test Compound	Molecular weight	LogP	$_{P}k_a$ (acid)	$_{P}k_a$ (base)
Sunitinib	398.473	3.24	11.46	9.04
Imatinib	493.602	3.47	12.45	8.27
Nilotinib	529.515	4.51	12.38	5.92
Dasatinib	488.000	2.77	8.49	7.22
benzethonium	412.637	3.13	17.31	-4.10