

INTRODUCTION AND AIMS

- Hypertension is a major preventable cause of morbidity and mortality in the U.K. which affects over one in four adults¹.
- Despite this it is thought that blood pressure is optimally controlled in only 50-66% of patients².
- Furthermore, it is estimated that around 25% of patients are non-adherent to anti hypertensive therapy³.

Initial NHS Lothian pilot audit data:

Clinic data - demographics

Total tests: $n = 14$

Females: $n = 7$

Age: 69 ± 7

Average number of drugs: $n = 4$

Total tests: $n = 14$

Adherent patients: $n = 9$ (64%)
3 patients discharged

Partially adherent: $n = 3$ (21%)

Drug Prescribed: 4, 4, 3

Drugs Detected: 3, 2, 1

Non-adherent: $n = 2$ (14%)

Aim:

To develop and validate a qualitative LC-MS/MS method for 29 anti hypertensive drugs in urine in line with the NHS Lothian Formulary.

METHOD

Sample Preparation

Protein Crash:

- 100 μ L of sample + 200 μ L Internal Standard + ZnSO₄
- Spin for 5 minutes at 2000 rpm
- Transfer 350 μ L of supernatant to glass vial

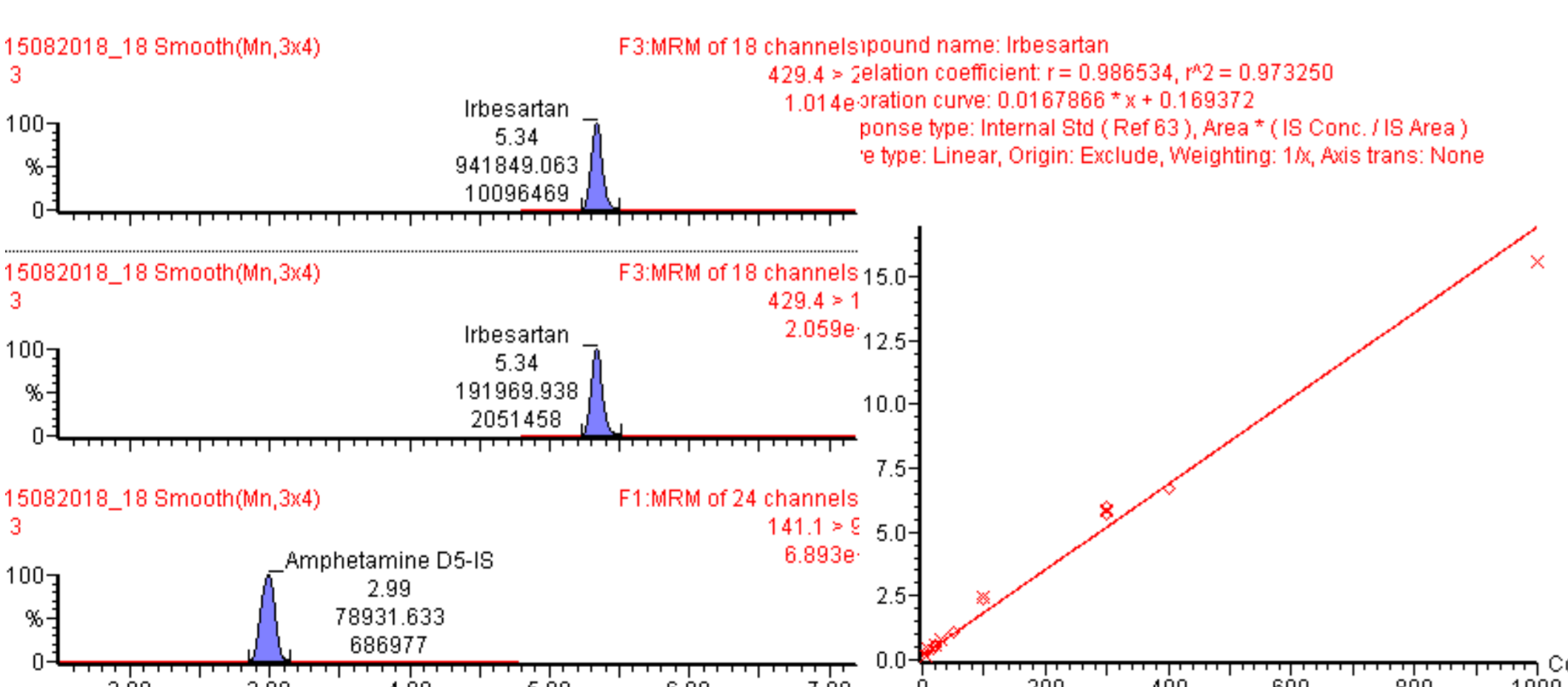


Figure 1 – Representative patient urine chromatogram from urine antihypertensive drug screening method (Irbesartan).

REFERENCES

- WHO. A global brief hypertension. www.internationalcardiovascular_diseases/publications/global_brief_hypertension. [Accessed November 2017]
- Tomaszewski M, White C, Patel P et al. High rates of non-adherence to antihypertensive treatment revealed by high-performance liquid chromatography-tandem mass spectrometry (HP LC-MS/MS) urine analysis. *Heart* 2013; 0: 1-7.
- Gupta P, Prashanth P, Strauch B, et al. Biochemical Screening for Nonadherence Is Associated With Blood Pressure Reduction and Improvement in Adherence. *Hypertension* 2017; 70: 1042-1048.

RESULTS

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M.S. Drug Parameters and Assay Performance

Drug	Precursor ion (m/z) (ionization mode)	Collision energy	Quantifying ion	Cone voltage	Qualifying ion	Cone voltage	R ²	LLOQ* (μg/L)	Patient Urine?
Amiloride	230 (+)	35	171	18	101	40	0.971	20	Yes
Amlodipine	409.15 (+)	22	170	32	149	45	0.99	10	Yes
Atenolol	267.2 (+)	34	74	23	145.1	22	0.931	20	Yes
Bendroflumethiazide	421 (-)	53	329	20	290	20	0.997	100	Yes
Bisoprolol	326.25 (+)	24	56	38	89	50	0.984	10	Yes
Candesartan	441.2 (+)	28	192	4	207.2	30	0.975	10	Yes
Chlortalidone	337 (-)	44	190	14	-	-	0.995	100	No
Diltiazem	415.25 (+)	38	178	24	150	43	0.977	10	Yes
Doxazosin	452.2 (+)	70	344.3	30	98	50	0.94	10	Yes
Enalapril	377.2 (+)	36	234.2	20	160.2	30	0.998	10	Yes
Eplerenone	415.25 (+)	28	163	18	55	60	0.99	10	Yes
Felodipine	384.1 (-)	20	338.1	9	324	27	0.965	20	Yes
Furosemide	329 (+)	27	204.7	22	285.2	15	0.993	100	No
Hydrochlorthiazide	296 (-)	58	208.1	23	126	35	1.0	400	No
Indapamide	366 (+)	33	132	22	-	-	0.993	10	Yes
Irbesartan	429.4 (+)	32	207.1	22	180.2	45	0.973	10	Yes
Labetalol	329.3 (+)	22	311.2	12	207.2	17	0.973	10	Yes
Lercanidipine	612.4 (+)	47	91.1	72	269.2	47	0.95	10	No
Lisinopril	406.2 (+)	43	84	40	91.1	57	0.993	10	Yes
Losartan	423.4 (+)	34	207	28	180	42	0.996	10	Yes
Metoprolol	268.3 (+)	41	191.2	20	116.1	20	0.963	10	No
Moxonidine	242.3 (+)	44	56.2	26	137.2	26	0.996	10	Yes
Nifedipine	347.1 (+)	33	254	22	211	22	0.99	10	Yes
Perindopril	369 (+)	36	172	22	98.1	44	0.992	10	Yes
Propranolol	260 (+)	44	116	19	183	17	0.93	10	Yes
Ramipril	417.3 (+)	44	234.2	26	-	-	0.997	10	No
Canrenone	341.5 (+)	50	107.2	30	83	44	0.981	10	Yes
Telmisartan	515 (+)	77	276.3	45	317.3	45	0.99	10	No
Verapamil	455.3 (+)	25	165	27	303.3	25	0.996	10	Yes

* Data reflects intra-assay precision

Rates of adherence in all hypertension patients:

Total tests: $n = 89$

Adherent patients: $n = 9$ (94%)

Partially adherent: $n = 3$ (21%)

Non-adherent: $n = 2$ (14%)

Rates of adherence in resistant hypertension patients:

Total tests: $n = 89$

Adherent patients: $n = 9$ (94%)

Partially adherent: $n = 3$ (21%)

Non-adherent: $n = 2$ (14%)

DISCUSSION AND FUTURE WORK

- Method validation for 22/29 drugs is complete.
- Rates of adherence are high in NHS Lothian
- Adherence is worse in resistant hypertension patients.
- A business case is underway to introduce the method as a routine service in NHS Lothian.
- Following introduction of the service compliance to medication will be re-audited.

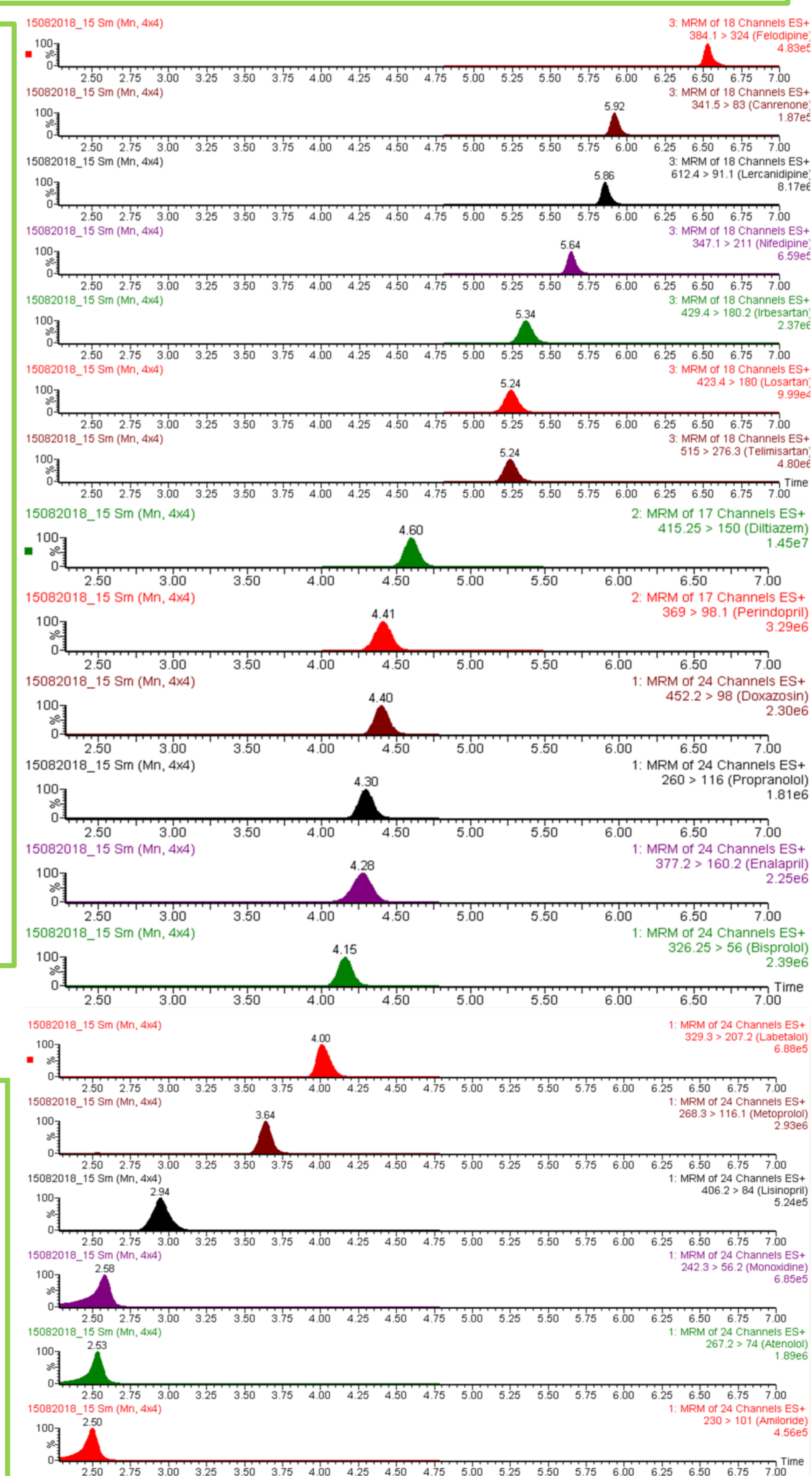


Figure 2 – Chromatographic separation of +ve spray drugs