DEVELOPMENT OF A SINGLE OPTIMIZED METHOD FOR THE HPLC ANALYSIS OF ANGIOTENSIN II RECEPTOR BLOCKER (ARB) ANTAGONISTS.

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Objective 1 -
To optimise Assay and Related Substances HPLC methods for irbesartan, losartan and valsartan
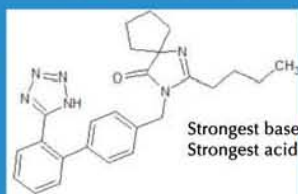
Objective 2 -
To use the strategy adopted in Objective 1 to develop an Assay Method that resolves the three APIs in a single reverse phase HPLC method
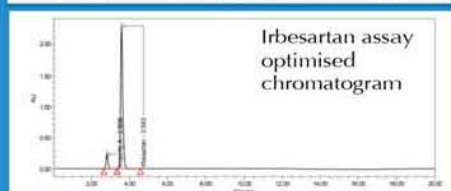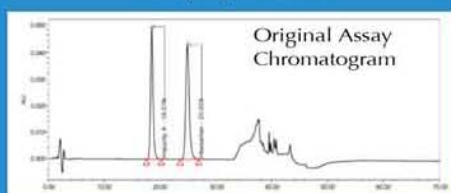
Objective 3 -
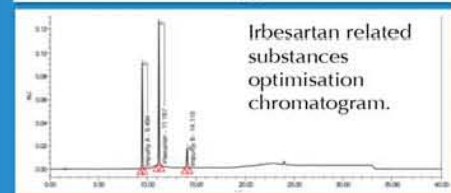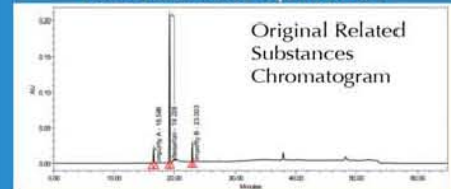To transfer the method developed in Objective 2 from HPLC to UPLC

Irbesartan

Strongest base pKa = 4.20
Strongest acid pKa = 7.40

Assay Optimisation

Original Assay Chromatogram

Irbesartan assay optimised chromatogram

Related Substance Optimisation

Original Related Substances Chromatogram

Irbesartan related substances optimisation chromatogram.

Valsartan

Strongest base pKa = -0.11
Strongest acid pKa = 4.37

Assay Optimisation

Original Assay Chromatogram for Valsartan

Valsartan Assay optimised chromatogram

Related Substance Optimisation

Original Related Substances Chromatogram for Valsartan

Valsartan related substances optimisation chromatogram

Losartan

Strongest base pKa = 4.12
Strongest acid = 7.4

Assay and Related Substances Optimisation

Original Assay Chromtogram for Losartan

Original Related Substances Chromatogram for Losartan

Combined Method Optimisation

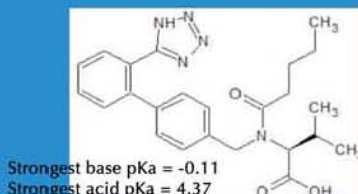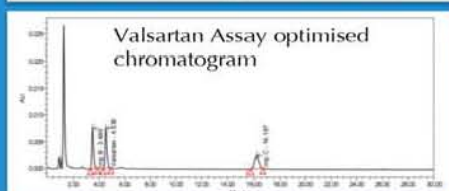Losartan Assay and Related Substances optimisation chromatogram
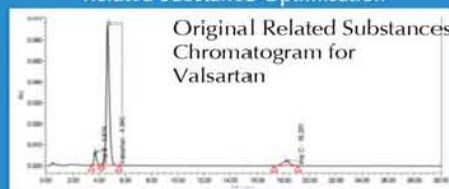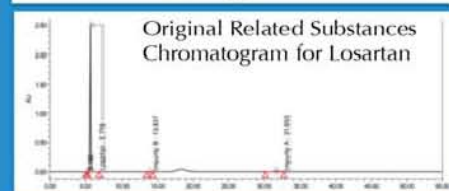
Method Development

Developed HPLC Assay

Method transferred to UPLC
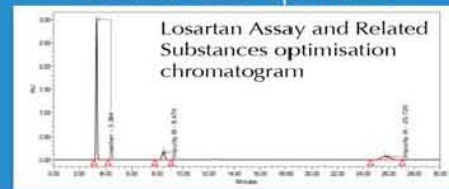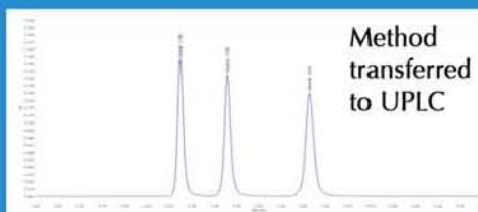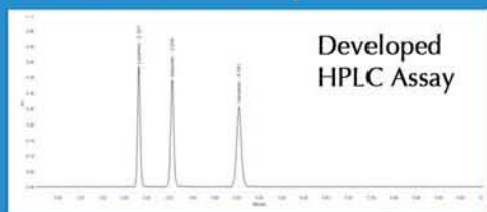
Peak Name	RRT in HPLC	RRT in UHPLC
Losartan	1.00	1.00
Irbesartan	1.32	1.32
Valsartan	1.96	1.90

Obtaining close RRT (Relative Retention times) between the two methods signifies that the geometrical transfer was executed successfully and that the two methods could be used interchangeably and the results compared with each other.

Peak Name		Retention Time (min)	Area	Capacity Factor	Resolution	Tailing Factor	Plate Count	Height (µV)
Losartan	Mean	2.319	1649066.4	3.639	N/A	1.033	7072	386610.4
	%RSD	0.09%	0.1%	0.12%	N/A	0.4%	0.96%	0.16%
Irbesartan	Mean	3.072	1748992	5.144	6.234	0.992	8803	344159.5
	%RSD	0.1%	0.1%	0.12%	0.29%	0.21%	0.47%	0.19%
Valsartan	Mean	4.535	1908869.3	8.071	9.084	1.03	8867	253824.2
	%RSD	0.13%	0.12%	0.15%	0.25%	0.08%	0.52%	0.25%

Peak Name		Retention Time (min)	Area	Capacity Factor	Resolution	Tailing Factor	Plate Count	Height (µV)
Losartan	Mean	0.324	164755.6	2.237	N/A	1.19	3683	187827.6
	% RSD	0.19%	0.20%	0.27%	N/A	0.44	1.14	0.44
Irbesartan	Mean	0.428	174542.2	3.28	4.465	1.106	4505	165219.7
	% RSD	0.17%	0.67%	0.22%	0.30%	0.17%	0.72%	0.42%
Valsartan	Mean	0.614	189376.3	5.135	6.363	1.089	5547	139763.8
	% RSD	0.10%	0.34%	0.12%	0.63%	0.31%	0.72%	0.38%