Supporting Information

Synthesis and Pharmacological Evaluation of a Selected Library of New Potential Anti-Inflammatory Agents Bearing the γ-hydroxybutenolide Scaffold: a New Class of Inhibitors of Prostanoid Production Through the Selective Modulation of Microsomal Prostaglandin E Synthase-1 Expression (mPGES-1)

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Solvents
Solvent A: H_2O/0.1% TFA
Solvent B: CH_3CN/0.1% TFA

Pressure Limits
Minimum Pressure: 0 bar
Maximum Pressure: 400 bar

Auxiliary
Maximal Flow Ramp: 100.00 ml/min^2
Compressibility A: 50*10^-6/bar
Minimal Stroke A: Auto
Compressibility B: 115*10^-6/bar
Minimal Stroke B: Auto

Signal
MWD; Signal=280.16 nm; Reference=off

Method A: Jupiter C-18, 250 x 4.60mm, 5µ, 300 Å

Time [min]	Solv. A [%]	Solv. B [%]	Flow [ml/min]	Pressure [bar]
0.00	100.0	0.0	1.000	400
5.00	95.0	5.0	1.000	400
6.00	95.0	5.0	1.000	400
36.00	0.0	100.0	1.000	400
40.00	0.0	100.0	1.000	400
45.00	100.0	0.0	1.000	400
50.00	100.0	0.0	1.000	400

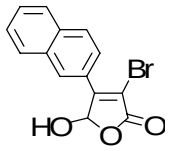
Method B: Jupiter C-4, 250 x 4.60mm, 5µ, 300 Å

Time [min]	Solv. A [%]	Solv. B [%]	Flow [ml/min]	Pressure [bar]
0.00	100.0	0.0	1.000	400
5.00	100.0	0.0	1.000	400
10.00	95.0	5.0	1.000	400
30.00	50.0	50.0	1.000	400
35.00	0.0	100.0	1.000	400
45.00	0.0	100.0	1.000	400
50.00	100.0	0.0	1.000	400
55.00	100.0	0.0	1.000	400

N. B. Negative peak at 4 min. is relative to the injection solvent (DMF) and that one at 45 min. is due to gradient change.

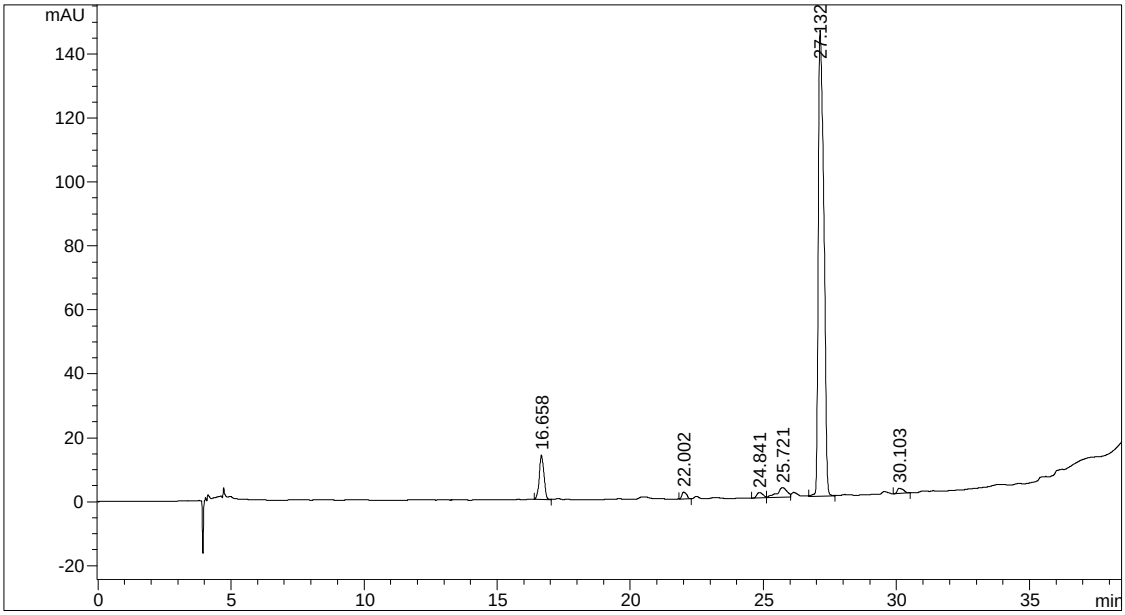
Compound	**Purity (%)**	
	Method A	Method B
4a	86.5	95.1
4b	100.0	99.9
4c	99.6	100.0
4d	99.8	99.9
4e	100.0	100.0
4f	83.6	94.1
4g	99.5	100.0
4h	95.9	96.9
4i	98.5	99.6

Table 1. Purity grade of compounds **4a-i** determined by HPLC

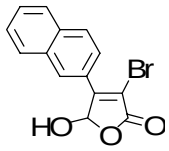


4a

Method A

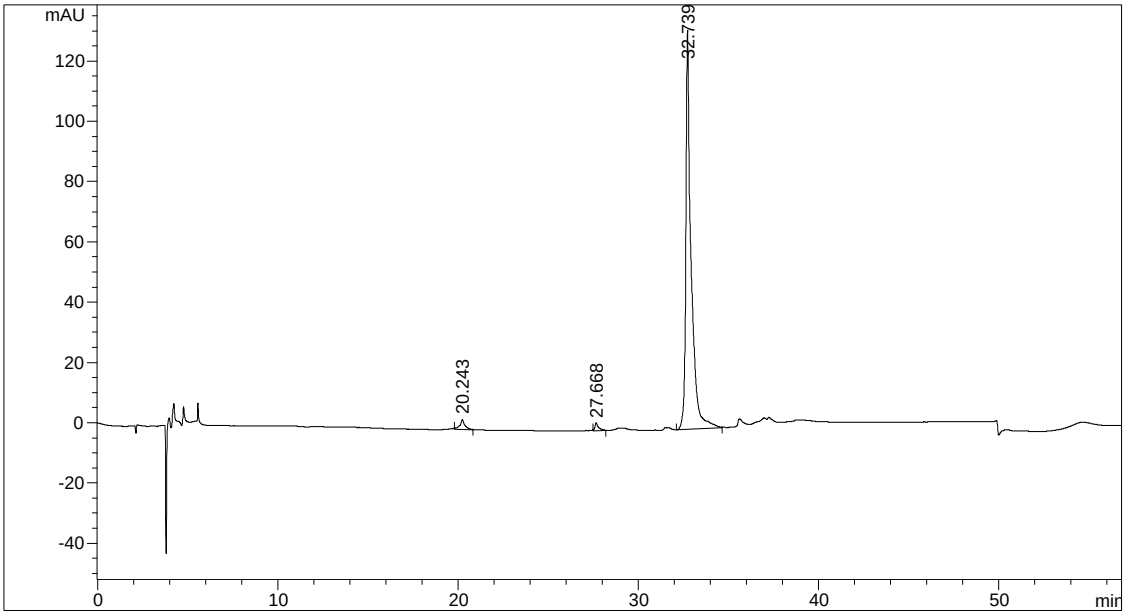


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.658	BB	0.1942	169.26079	13.88243	6.9060
2	22.002	BV	0.2068	26.60406	2.14402	1.0855
3	24.841	BV	0.2730	27.92094	1.70537	1.1392
4	25.721	VV	0.3857	81.44514	3.04801	3.3230
5	27.132	BB	0.2520	2120.06030	145.53247	86.5007
6	30.103	VB	0.2356	25.62592	1.62873	1.0456
Totals:				2450.91716	167.94102	

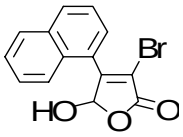


4a

Method B

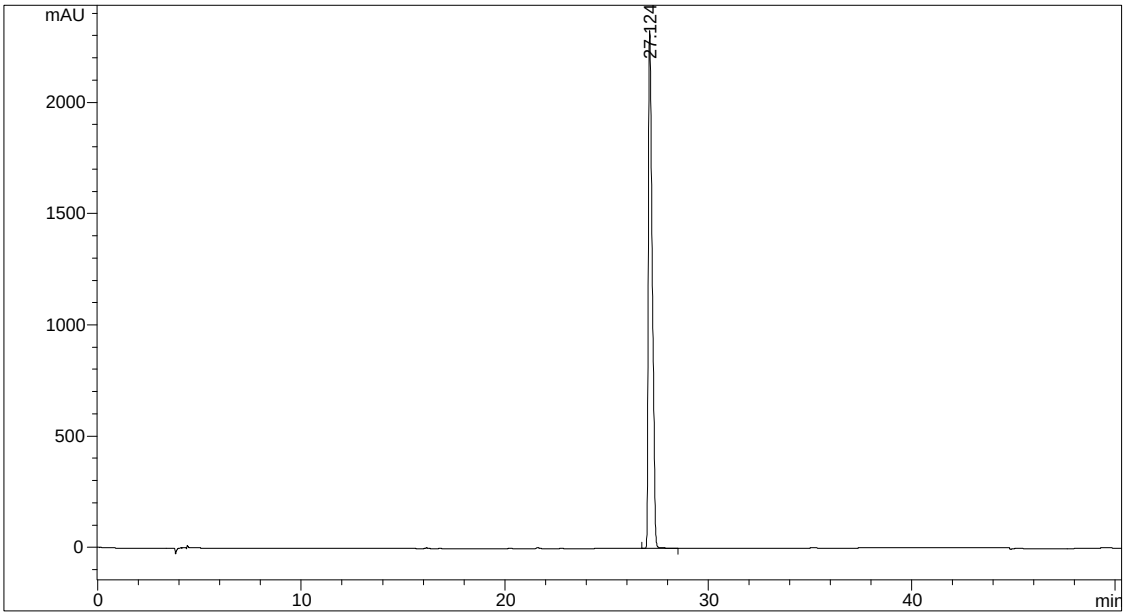


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.243	BB	0.3434	90.29146	3.42707	3.1932
2	27.668	BB	0.2325	47.11926	2.74186	1.6664
3	32.739	VB	0.2772	2690.16553	132.30035	95.1403
Totals:				2827.57625	138.46929	



4b

Method A



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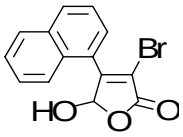
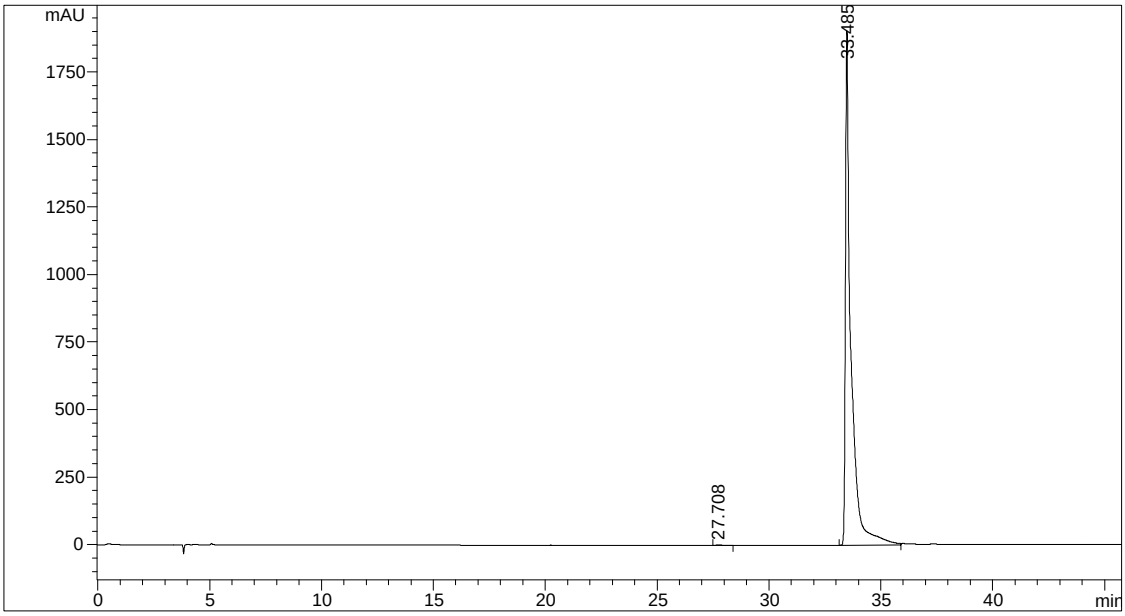
Totals:				3.10807e4	2325.34692	

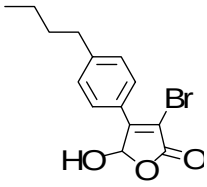


4b

Method B

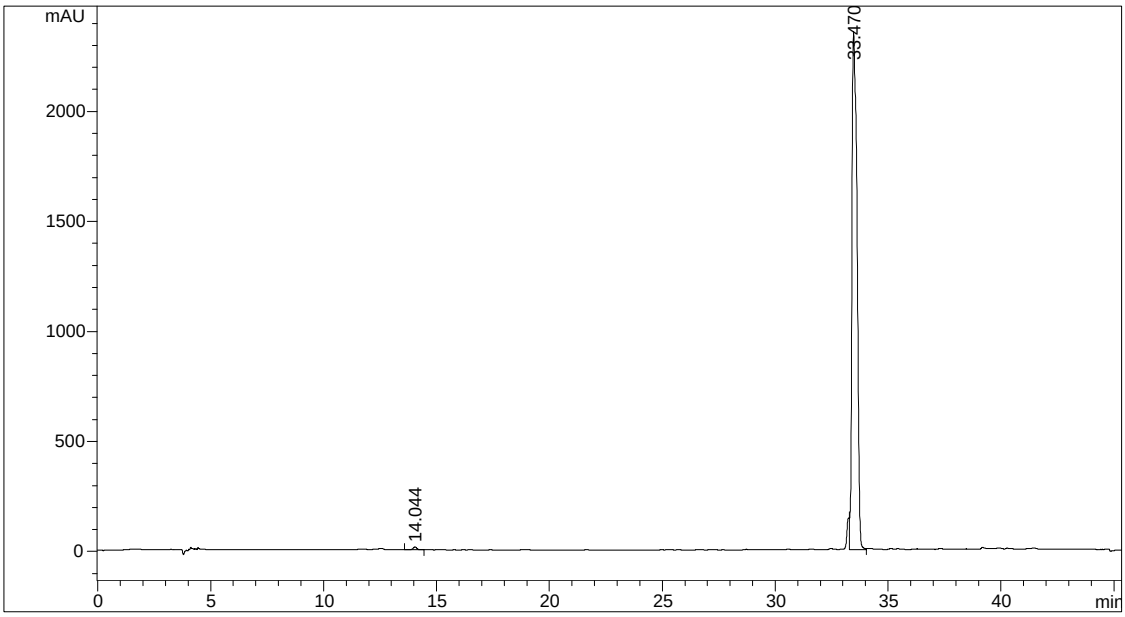


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.708	BB	0.1880	40.08339	2.88660	0.1235
2	33.485	BV	0.2286	3.24112e4	1903.93469	99.8765
Totals:				3.24513e4	1906.82129	

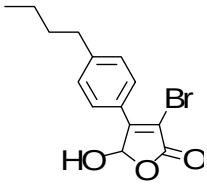


4c

Method A

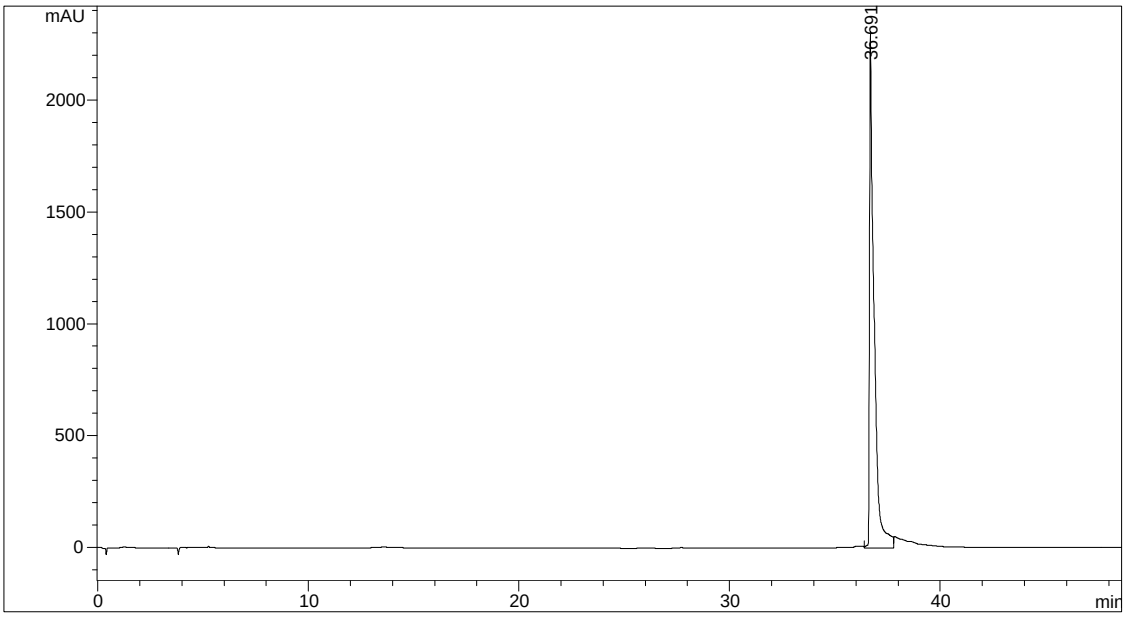


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.044	BB	0.1786	156.71184	12.99921	0.4238
2	33.470	VV	0.2607	3.68214e4	2353.62207	99.5762
Totals:				3.69781e4	2366.62128	

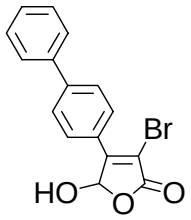


4c

Method B

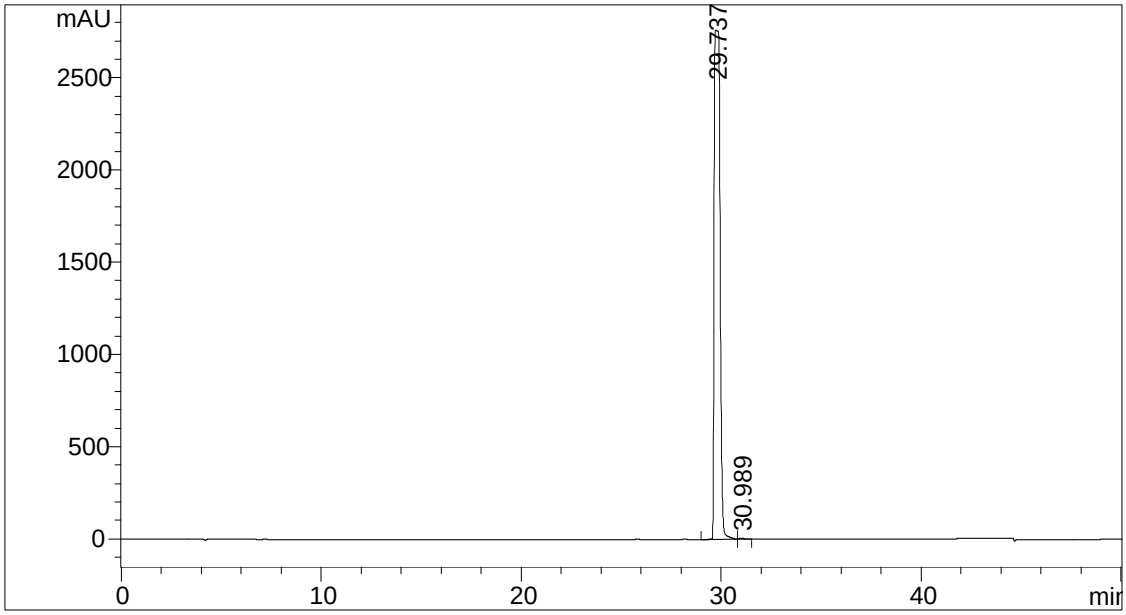


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.691	VV	0.1970	3.39573e4	2289.63721	100.0000
Totals:				3.39573e4	2289.63721	

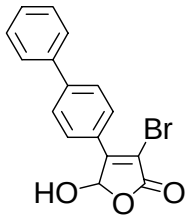


4d

Method A



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.737	BV	0.2699	5.58381e4	2761.65112	99.8129
2	30.989	VB	0.2735	104.68449	5.09921	0.1871
Totals:				5.59428e4	2766.75033	



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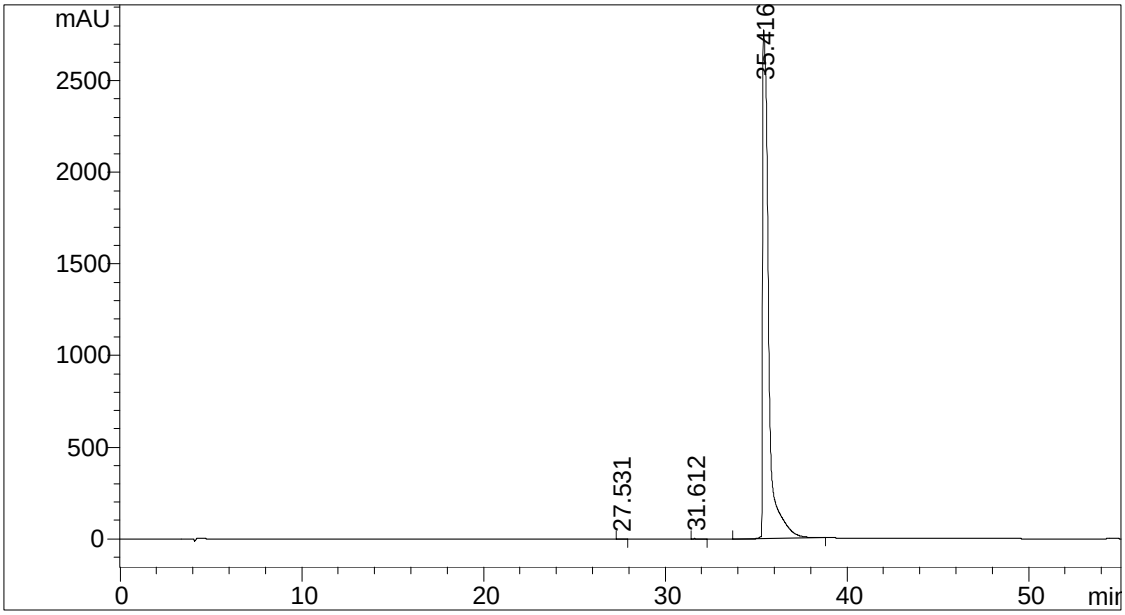
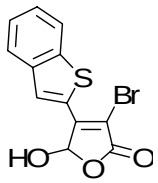
Method B

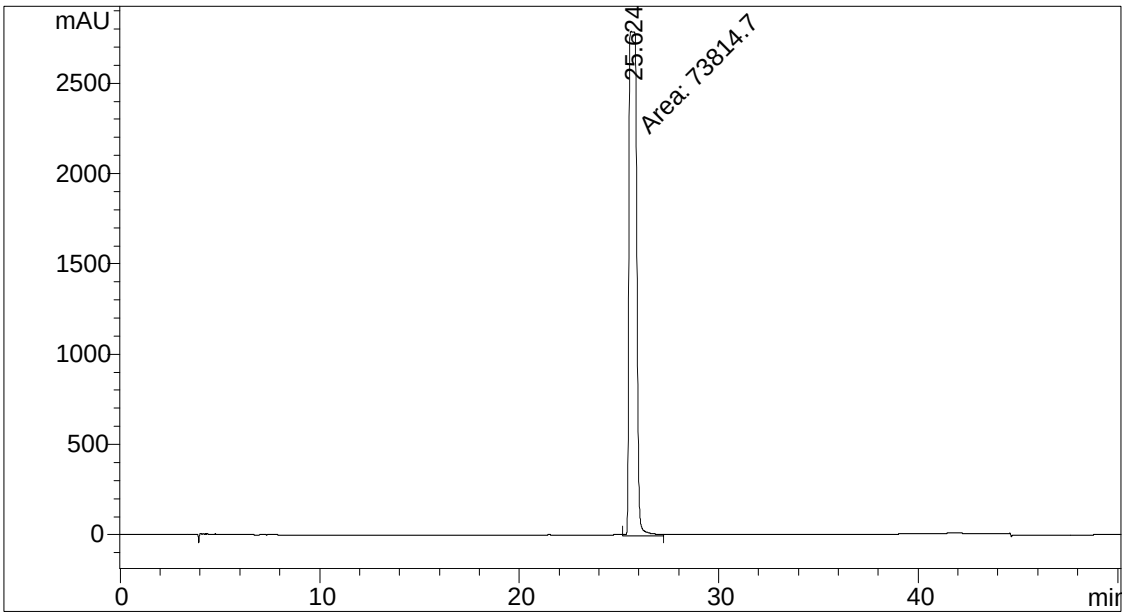


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.531	PB	0.1541	11.45380	1.05959	0.0178
2	31.612	PB	0.2420	42.25793	2.34769	0.0658
3	35.416	PB	0.3574	6.41355e4	2777.08887	99.9163
Totals:				6.41893e4	2780.49615	

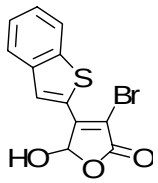


4e

Method A

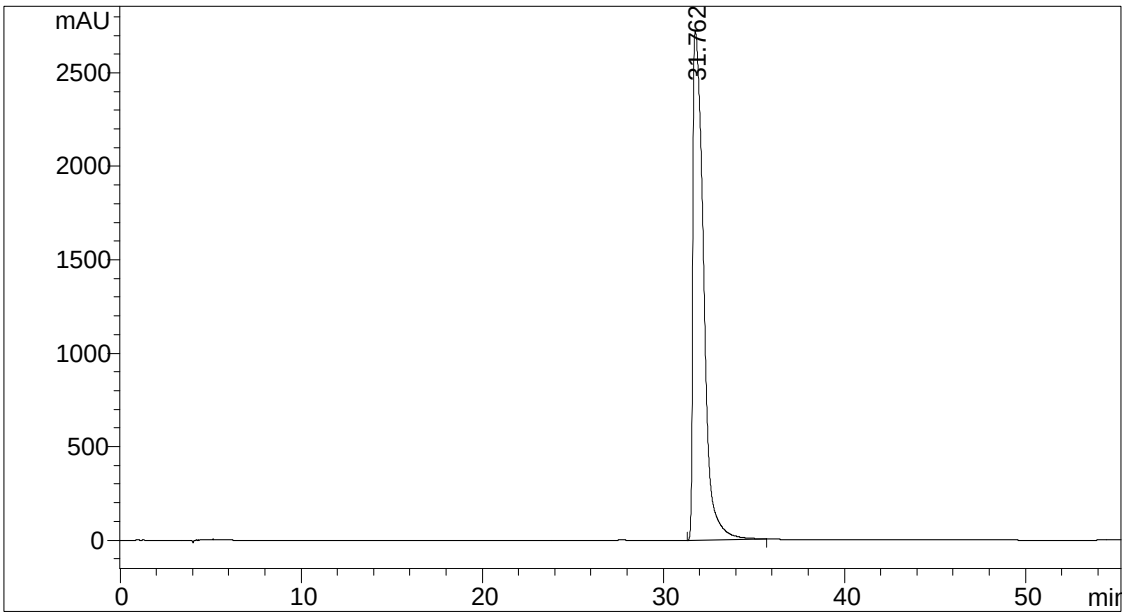


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.624	MM	0.4408	7.38147e4	2791.10547	100.0000
Totals:				7.38147e4	2791.10547	

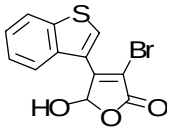


4e

Method B

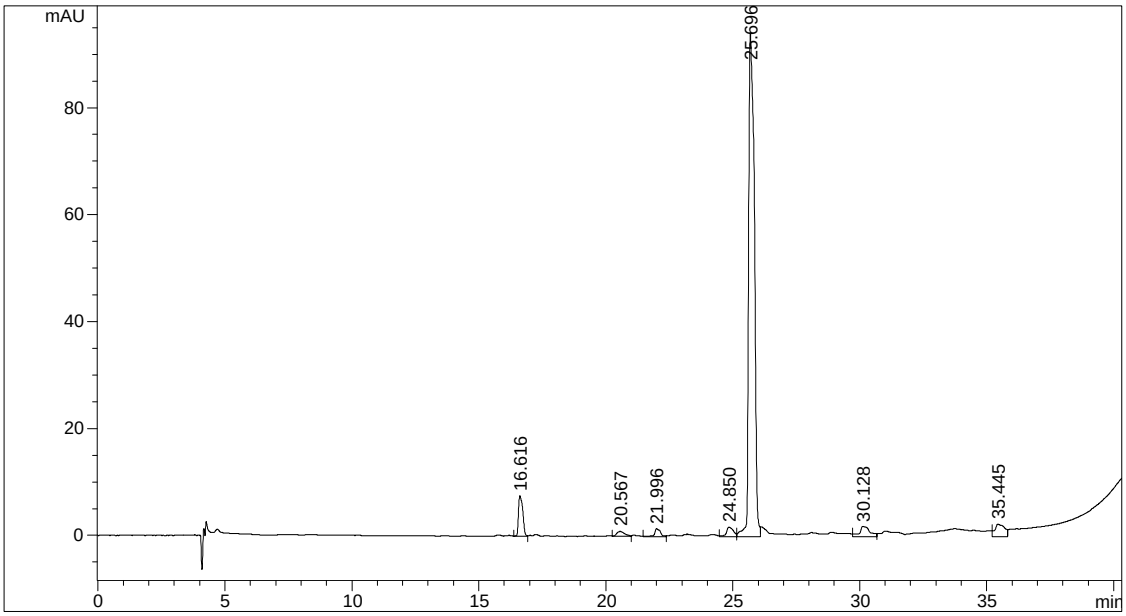


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.762	PB	0.6724	1.12085e5	2721.76929	100.0000
Totals:				1.12085e5	2721.76929	

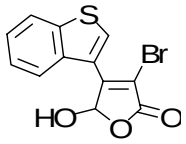


4f

Method A

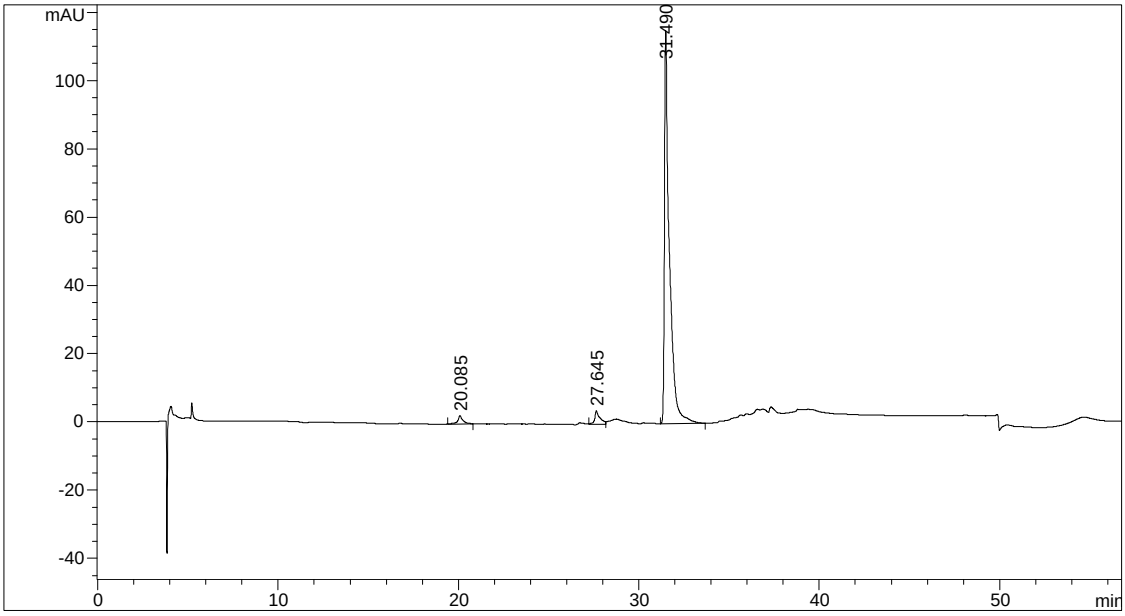


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.616	VV	0.1952	88.00045	7.59359	5.0576
2	20.567	BV	0.3451	21.77649	9.44086e-1	1.2515
3	21.996	VV	0.2138	23.34921	1.45038	1.3419
4	24.850	VV	0.3058	33.57772	1.75057	1.9298
5	25.696	VV	0.2118	1454.11450	94.32909	83.5710
6	30.128	VV	0.3612	55.45368	1.95342	3.1870
7	35.445	BV	0.3443	63.70332	2.36451	3.6612
Totals:				1739.97536	110.38564	

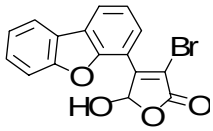


4f

Method B

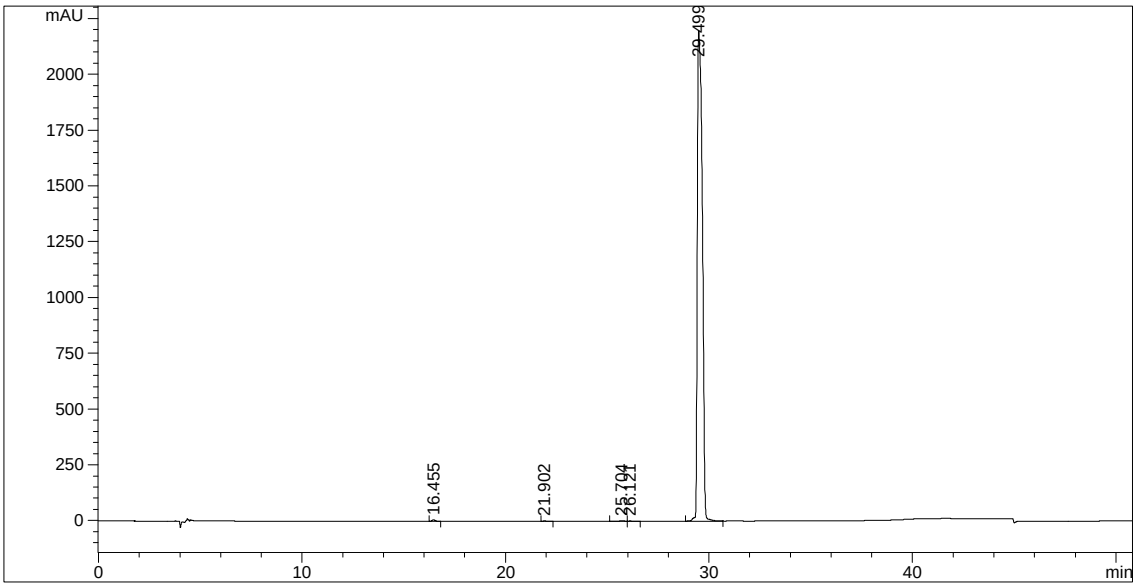


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.085	BB	0.2785	52.27445	2.51449	2.2407
2	27.645	BV	0.2825	84.69088	4.00895	3.6301
3	31.490	BB	0.2588	2196.02515	115.01468	94.1292
Totals:				2332.99048	121.53812	

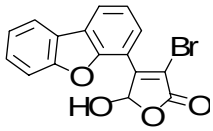


4g

Method A

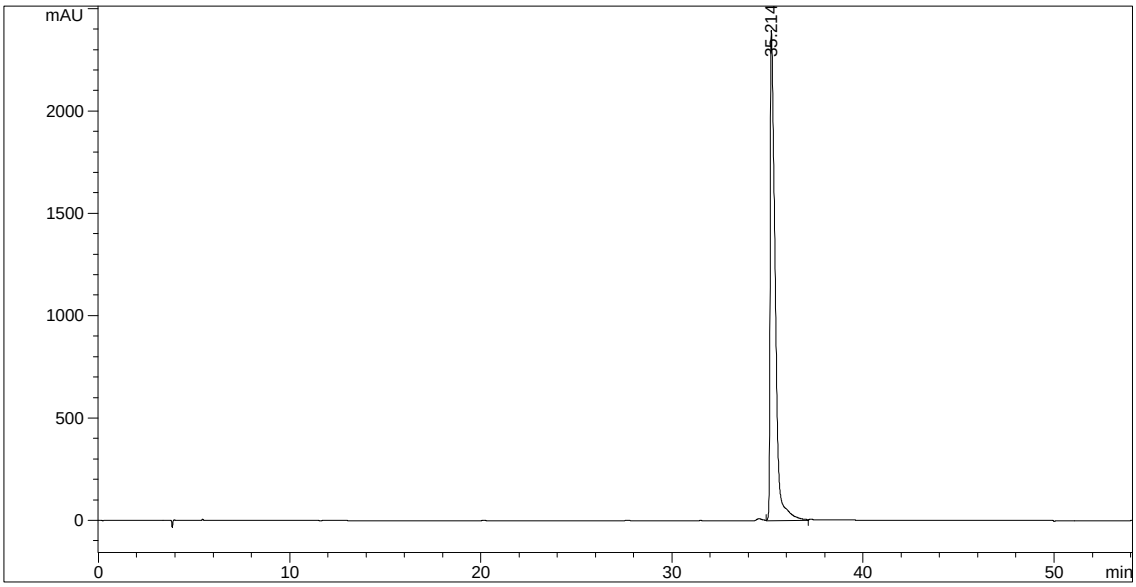


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.455	BP	0.1801	83.01142	7.55965	0.2211
2	21.902	BP	0.2050	25.78043	2.13242	0.0687
3	25.704	VV	0.3185	49.11239	2.40235	0.1308
4	26.121	VB	0.2455	22.42845	1.39588	0.0597
5	29.499	BB	0.2924	3.73611e4	2196.57690	99.5196
Totals:				3.75414e4	2210.06720	



4g

Method B



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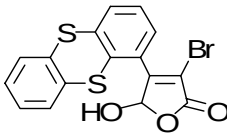
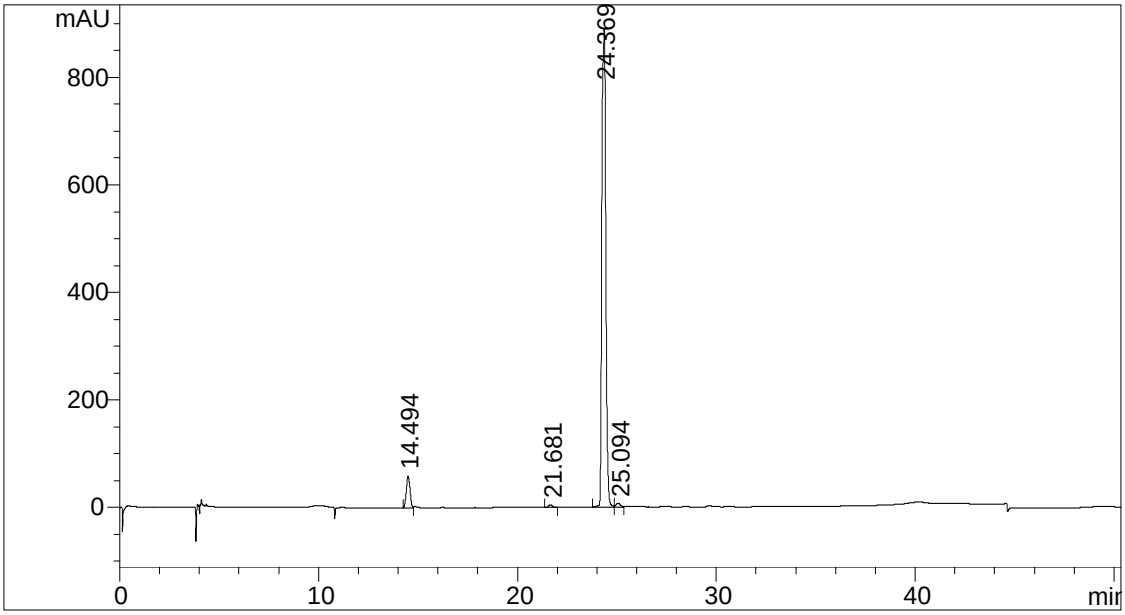
1	35.214	VV	0.2568	4.36667e4	2393.53711	100.0000
Totals :				4.36667e4	2393.53711	

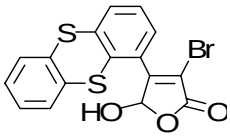


4h

Method A

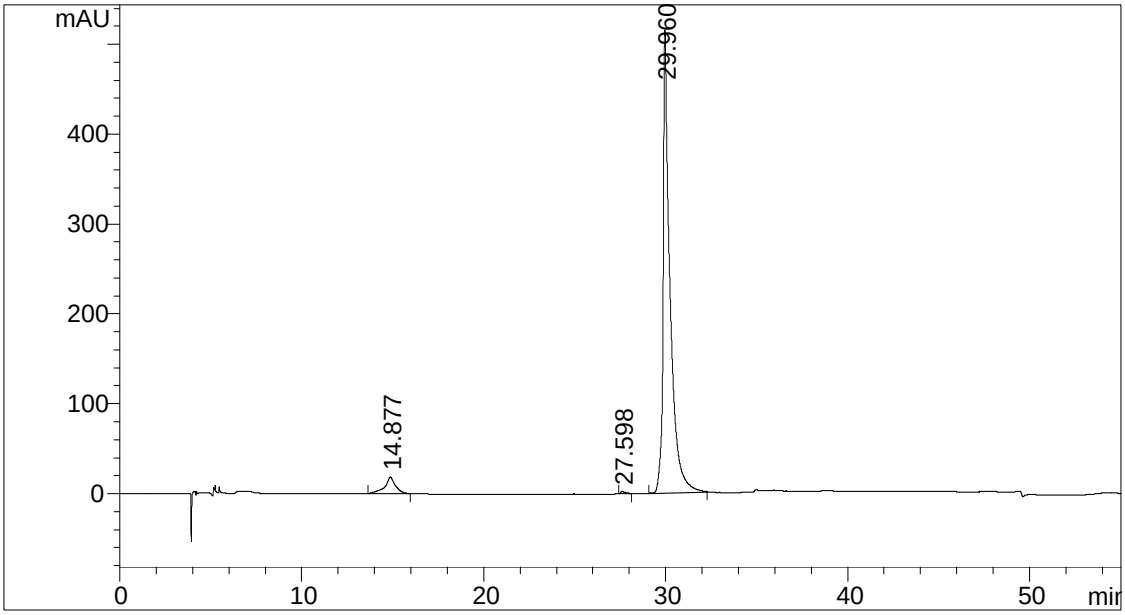


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.494	BV	0.2067	251.70784	19.48770	2.5942
2	21.680	VP	0.1661	90.46669	7.42807	0.9324
3	24.369	VV	0.2264	9305.82422	668.66150	95.9084
4	25.093	VV	0.2261	54.82903	3.22915	0.5651
Totals:				9702.82778	698.80641	

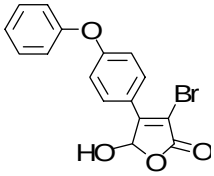


4h

Method B

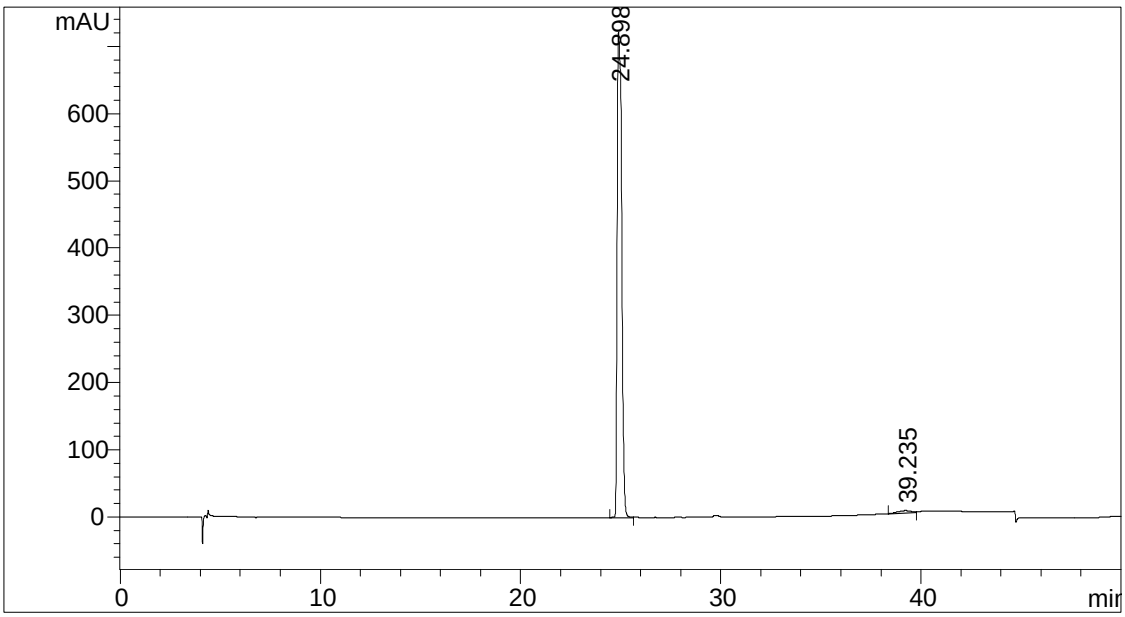


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.876	BB	0.4957	228.57838	6.14824	2.1493
2	27.601	BB	0.2693	101.47100	4.94631	0.9541
3	29.961	BB	0.3457	1.03050e4	393.27533	96.8966
Totals:				1.06351e4	404.36988	

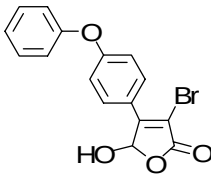


4i

Method A

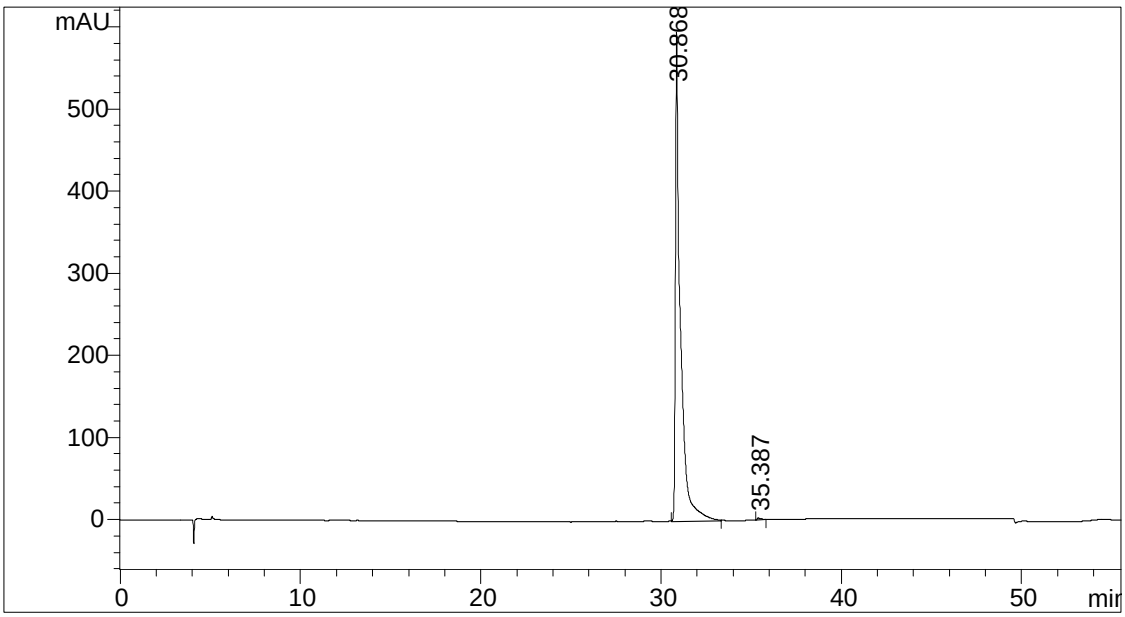


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.898	BB	0.2189	1.14466e4	722.23309	98.5369
2	39.235	BV	0.6156	169.96167	3.63432	1.4631
Totals:				1.16165e4	725.86741	



4i

Method B



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.868	BB	0.2535	1.13089e4	595.70148	99.6056
2	35.387	BB	0.2236	44.78064	2.61790	0.3944
Totals:				1.13537e4	598.31937	