

## Supporting Information to

**Synthesis and Characterization of Potential Dimers of  
Gatifloxacin – an Antibacterial Drug****Srinivas GARAGA, Ambati V. RAGHAVA REDDY, Koilpillai Joseph PRABAHAR,  
Raghu Babu KORUPOLU, Paul Douglas SANASI**

Published in Sci Pharm. 2013; 81: 651–662

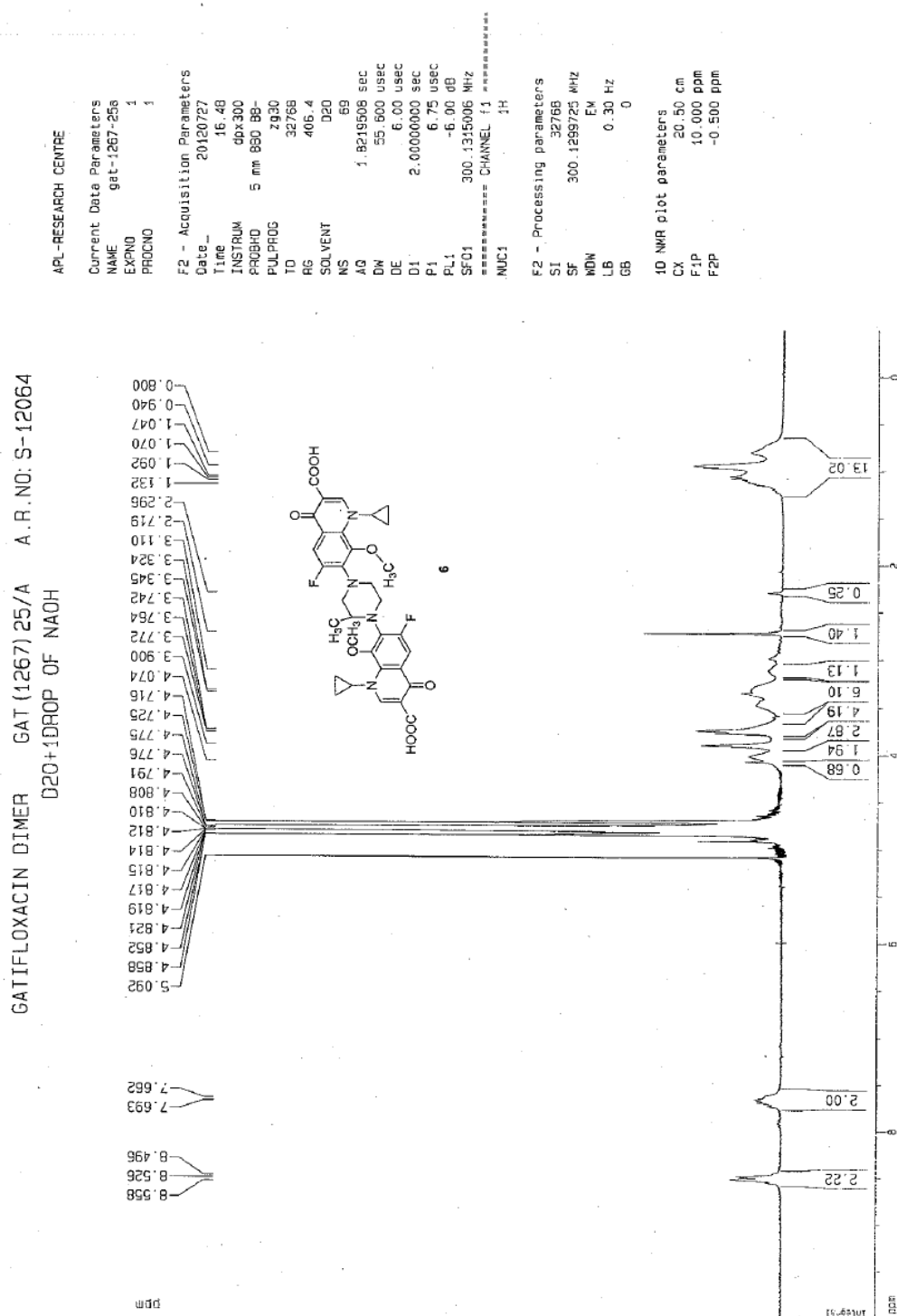
doi:10.3797/scipharm.1212-21

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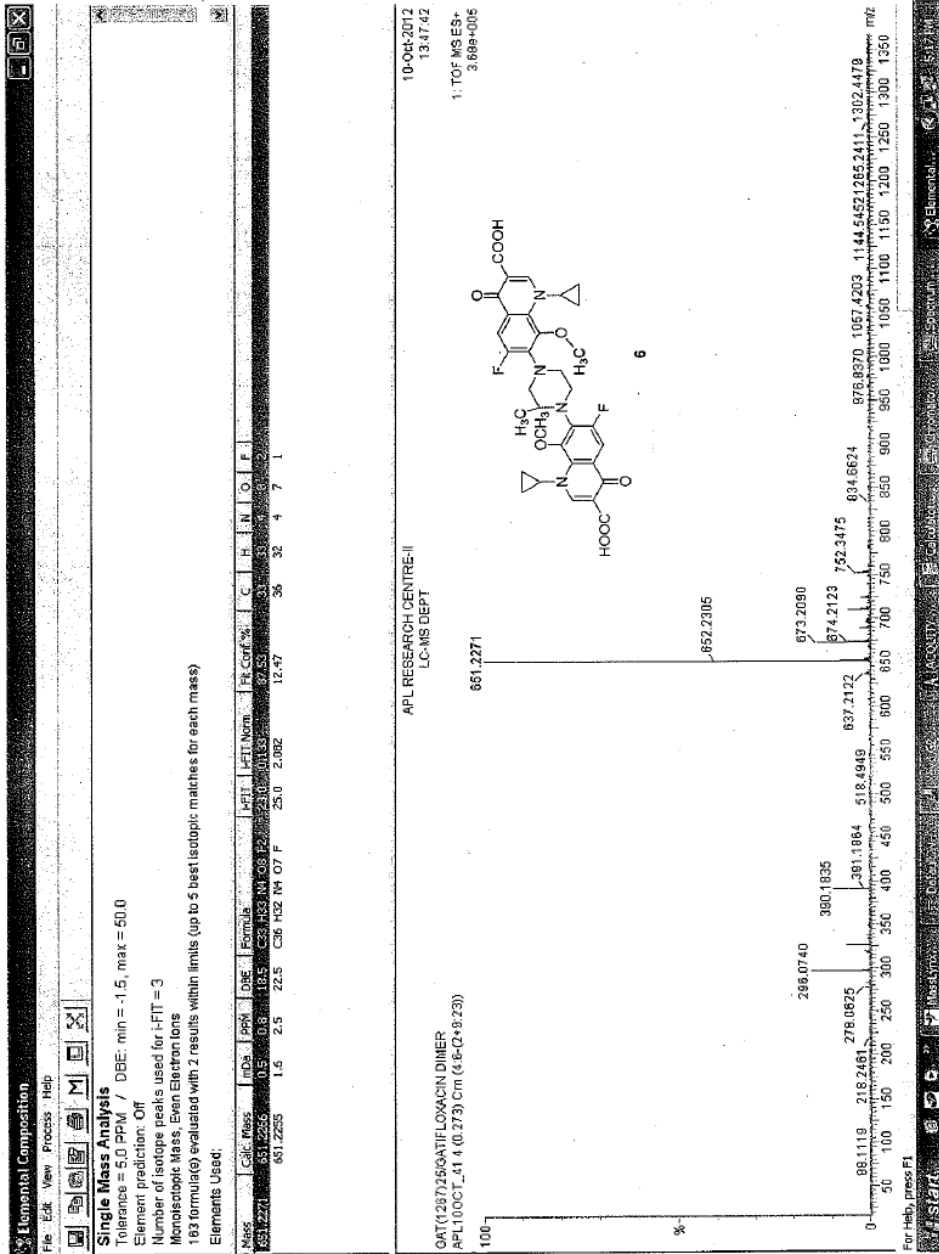
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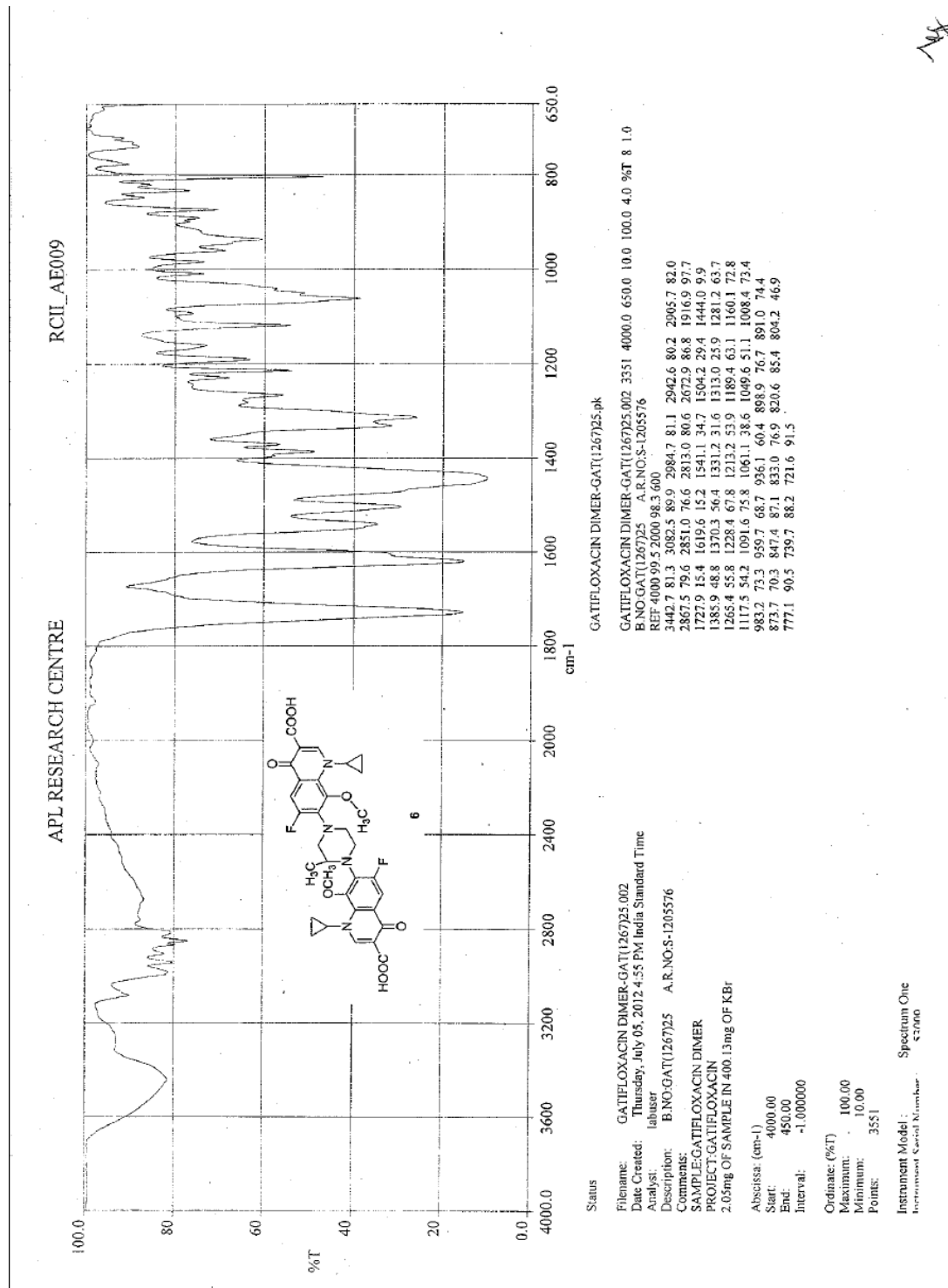
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**<sup>1</sup>H-NMR of Compound 6**

**HRMS & Elemental analysis of Compound 6**



IR Spectrum of Compound 6



**HPLC purity of Compound 6**

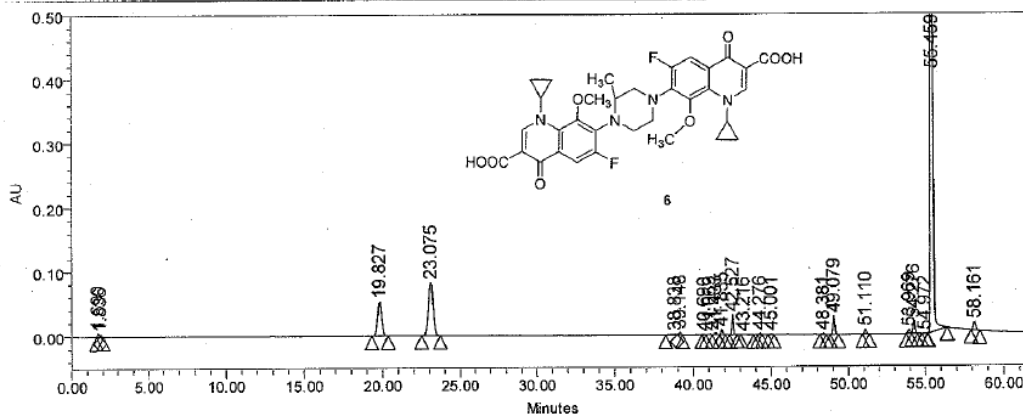
**APL RESEARCH CENTRE  
ANALYTICAL RESEARCH DEPARTMENT**

INSTRUMENT ID : RCIL\_AE136

PROJECT NAME : SEP\_2012\RCIL\_AE136

Sample ID : GAT(1267)25/Gatifloxacin  
Dimer(M/Z=650)  
Run Time : 72.0 Minutes  
Vial : 8  
Injection : 1  
Injection Volume : 20.00 ul

Proc. Chnl. Descr : PDA 293.0 nm  
Date Acquired : 9/18/2012 11:06:53 AM IST  
Acq. Method Set : Gatifloxacin\_RS  
Date Processed : 9/18/2012 12:23:02 PM IST  
Processing Method : Gatifloxacin\_RS\_Pro



**Peak Results**

	RT (min)	Area (μV*sec)	% Area	Name
1	1.69	47161	0.21	Peak24
2	1.84	22212	0.10	Peak25
3	19.83	988357	4.49	Peak26
4	23.07	1773743	8.05	Peak27
5	38.84	30405	0.14	Peak28
6	39.15	38609	0.18	Peak29
7	40.69	2126	0.01	Peak30
8	41.07	9778	0.04	Peak31
9	41.43	23563	0.11	Peak32
10	41.83	54284	0.25	Peak33
11	42.53	237251	1.08	Peak34
12	43.22	5236	0.02	Peak35
13	44.28	13769	0.06	Peak36
14	45.00	13153	0.06	Peak37
15	48.38	15729	0.07	Peak38
16	49.08	239113	1.09	Peak39

	RT (min)	Area (μV*sec)	% Area	Name
17	51.11	65212	0.30	Peak40
18	53.97	48154	0.22	Peak41
19	54.28	155592	0.71	Peak42
20	54.97	5371	0.02	Peak43
21	55.46	18107416	82.19	Peak44
22	58.16	135755	0.62	Peak45

**<sup>1</sup>H-NMR of Compound 9**

GATIFLOXACIN DIMER GAT (1267) 21 A.R.NO: S-011  
DMSO-d6

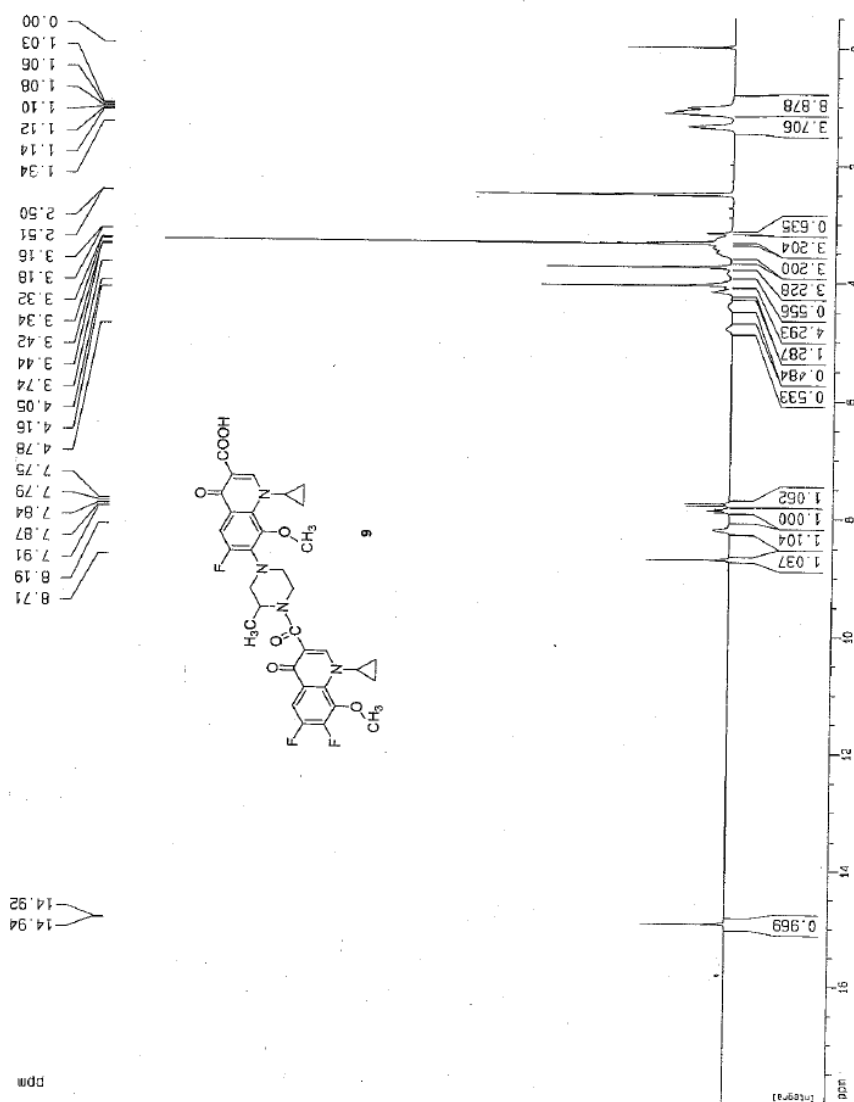
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 EXPNO 1  
 PROCNO 1

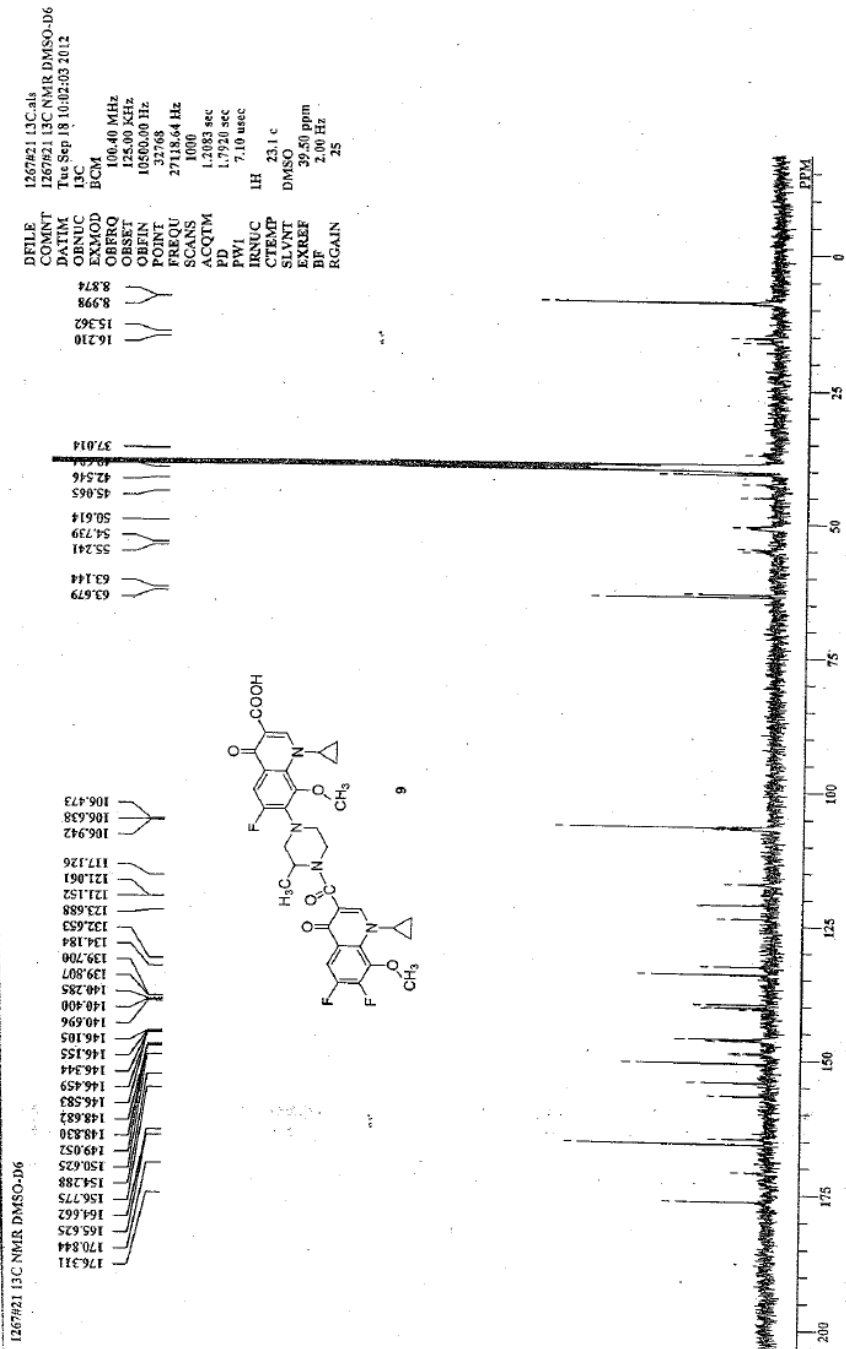
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 Time 15.26  
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 PROBHD 5 mm BBO BB-  
 PULPROG zg30  
 TD 32768  
 RG 645.1  
 SOLVENT DMSO  
 NS 49  
 AQ 1.8219508 sec  
 DW 55.600 usec  
 DE 6.00 usec  
 D1 2.00000000 sec  
 P1 6.75 usec  
 PL1 -6.00 dB  
 SF01 300.1315006 MHz  
 \*\*\*\*\* CHANNEL f1 \*\*\*\*\*  
 NUC1 <sup>1</sup>H

F2 - Processing parameters  
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 SF 300.1300003 MHz  
 MDW EM  
 LB 0.30 Hz  
 GB 0

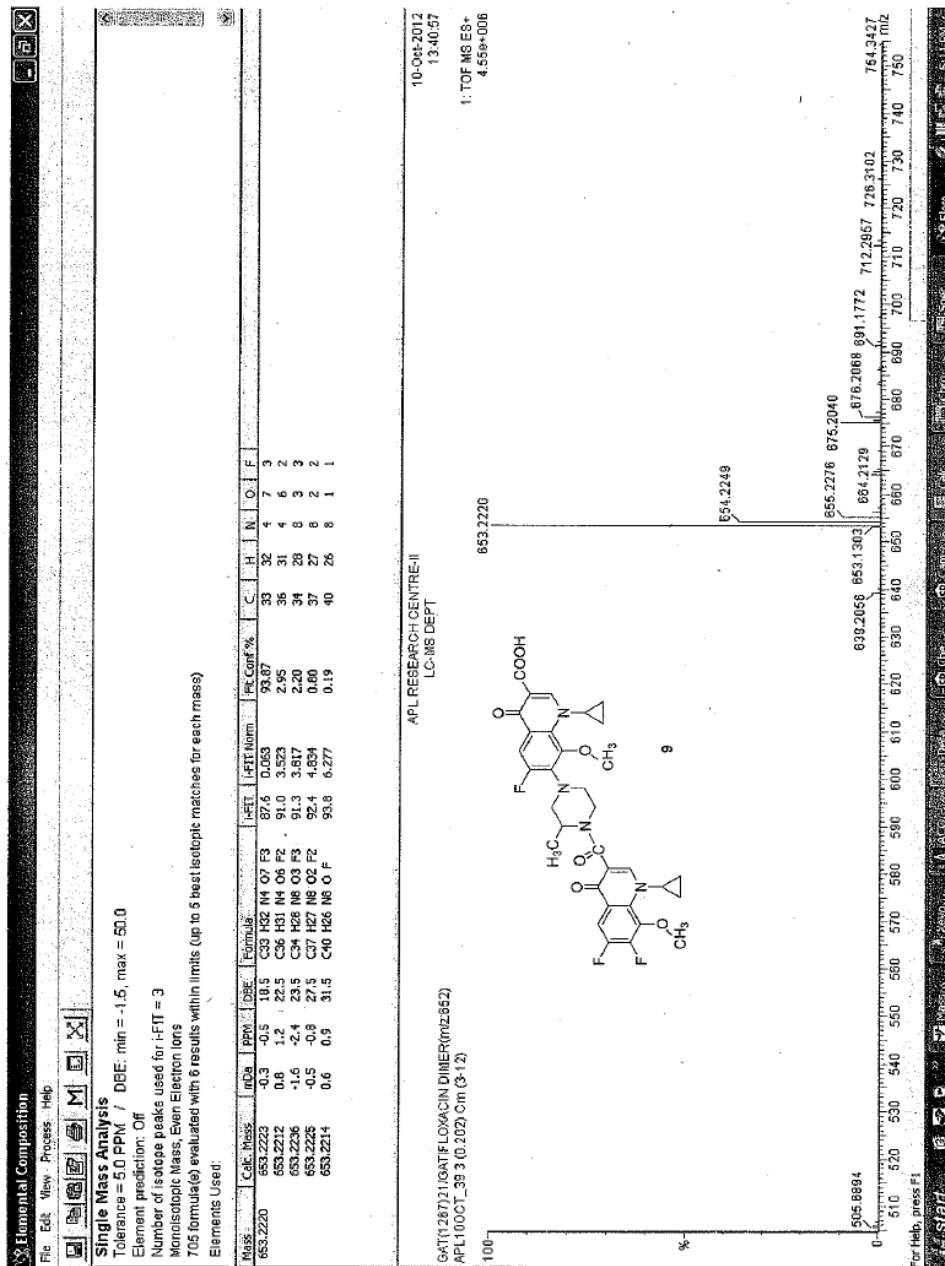
1D NMR plot parameters  
 CX 20.50 cm  
 F1P 18.000 ppm  
 F2P -0.500 ppm



<sup>13</sup>C-NMR of Compound 9

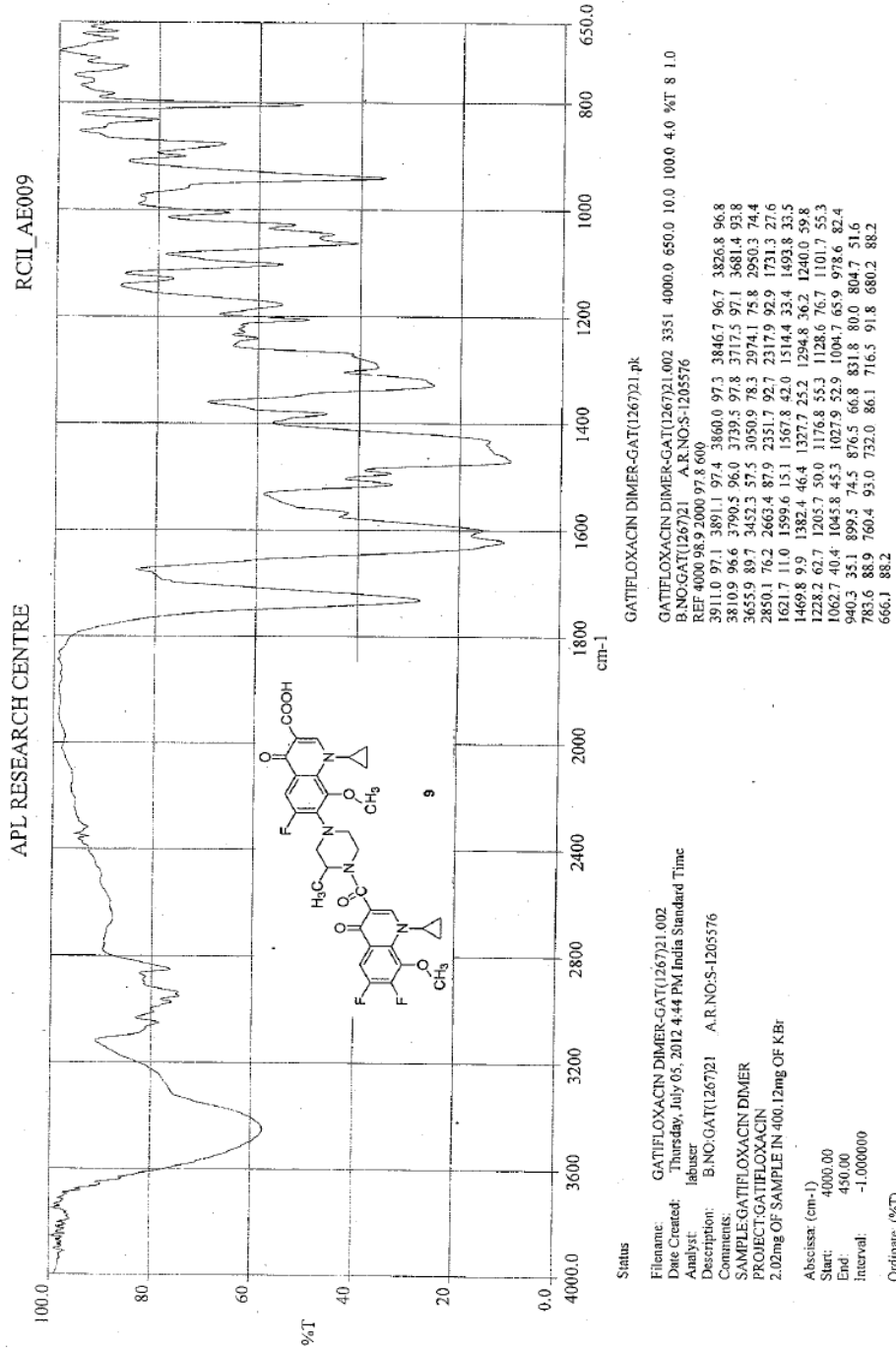


## HRMS &amp; Elemental analysis of Compound 9





IR Spectrum of Compound 9



MA

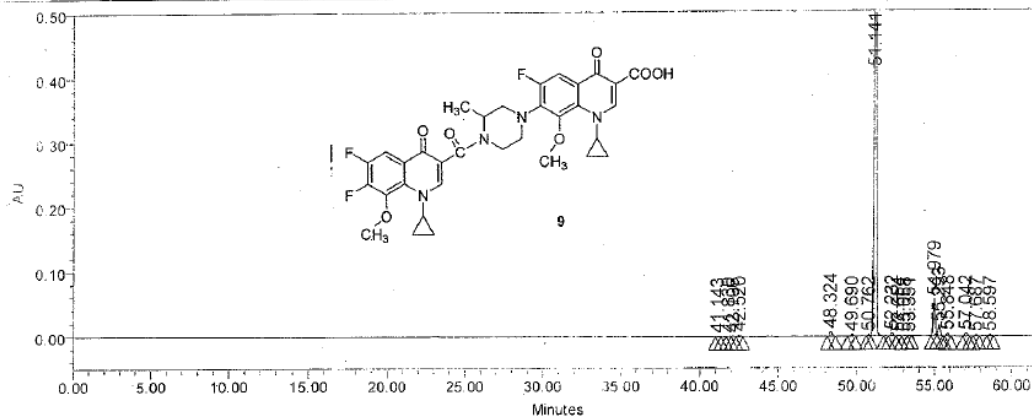
## HPLC Purity of Compound 9

**APL RESEARCH CENTRE  
ANALYTICAL RESEARCH DEPARTMENT**

INSTRUMENT ID: RCI\_AE136

PROJECT NAME: SEP\_2012\RCI\_AE136

Sample ID	GAT(1267)21/Gatifloxacin Dimer(M/Z=652)	Proc. Chnl. Descr	PDA 293.0 nm
Run Time	72.0 Minutes	Date Acquired	17/9/2012 19:01:30 IST
Vial	3	Acq. Method Set	Gatifloxacin_RS
Injection	1	Date Processed	18/9/2012 10:12:37 IST
Injection Volume	20.00 ul	Processing Method	Gatifloxacin_RS_Pro

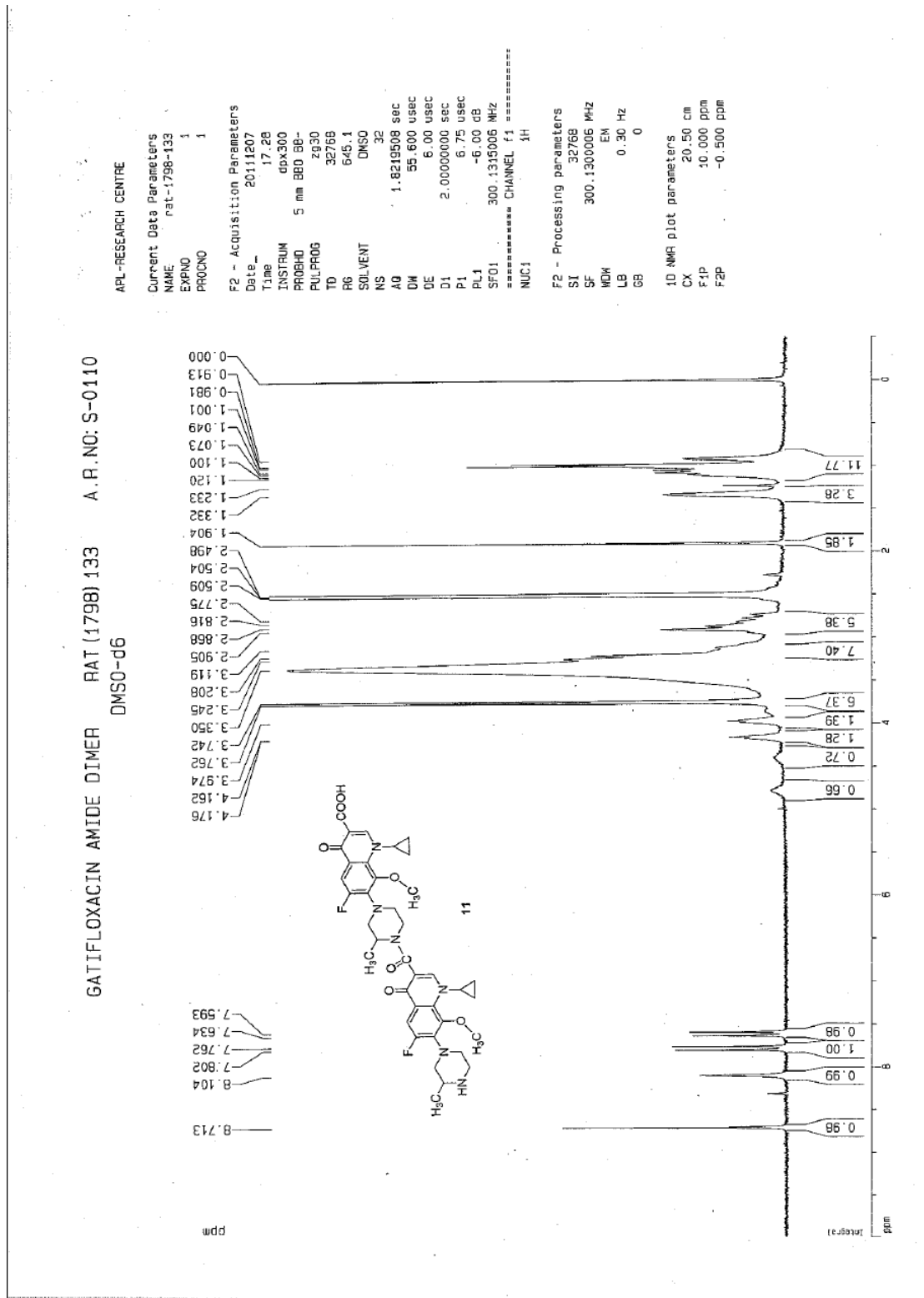


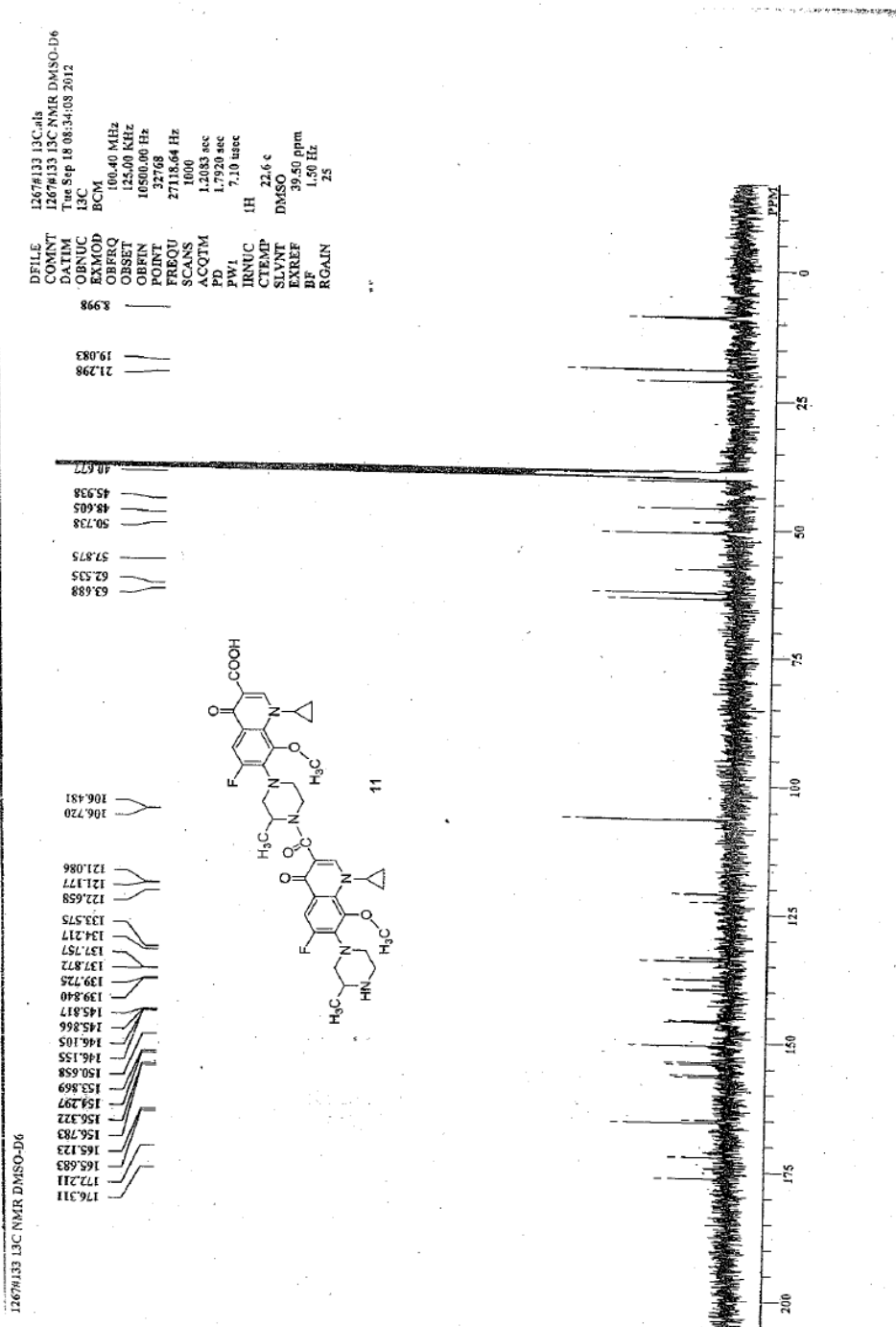
Peak Results

	RT (min)	Area (μV*sec)	% Area	Name
1	41.14	3860	0.04	Peak1
2	41.83	5788	0.05	Peak39
3	42.11	5346	0.05	Peak3
4	42.52	20900	0.19	Peak4
5	48.32	70927	0.65	Peak5
6	49.69	25733	0.23	Peak6
7	50.76	17748	0.16	Peak7
8	51.14	10064051	91.71	Peak8
9	52.23	37709	0.34	Peak9
10	52.65	6291	0.06	Peak10
11	53.06	3914	0.04	
12	53.35	3923	0.04	Peak11
13	54.98	488085	4.44	Peak12
14	55.29	120896	1.10	Peak13
15	55.85	31073	0.28	Peak14
16	57.04	35823	0.33	Peak15

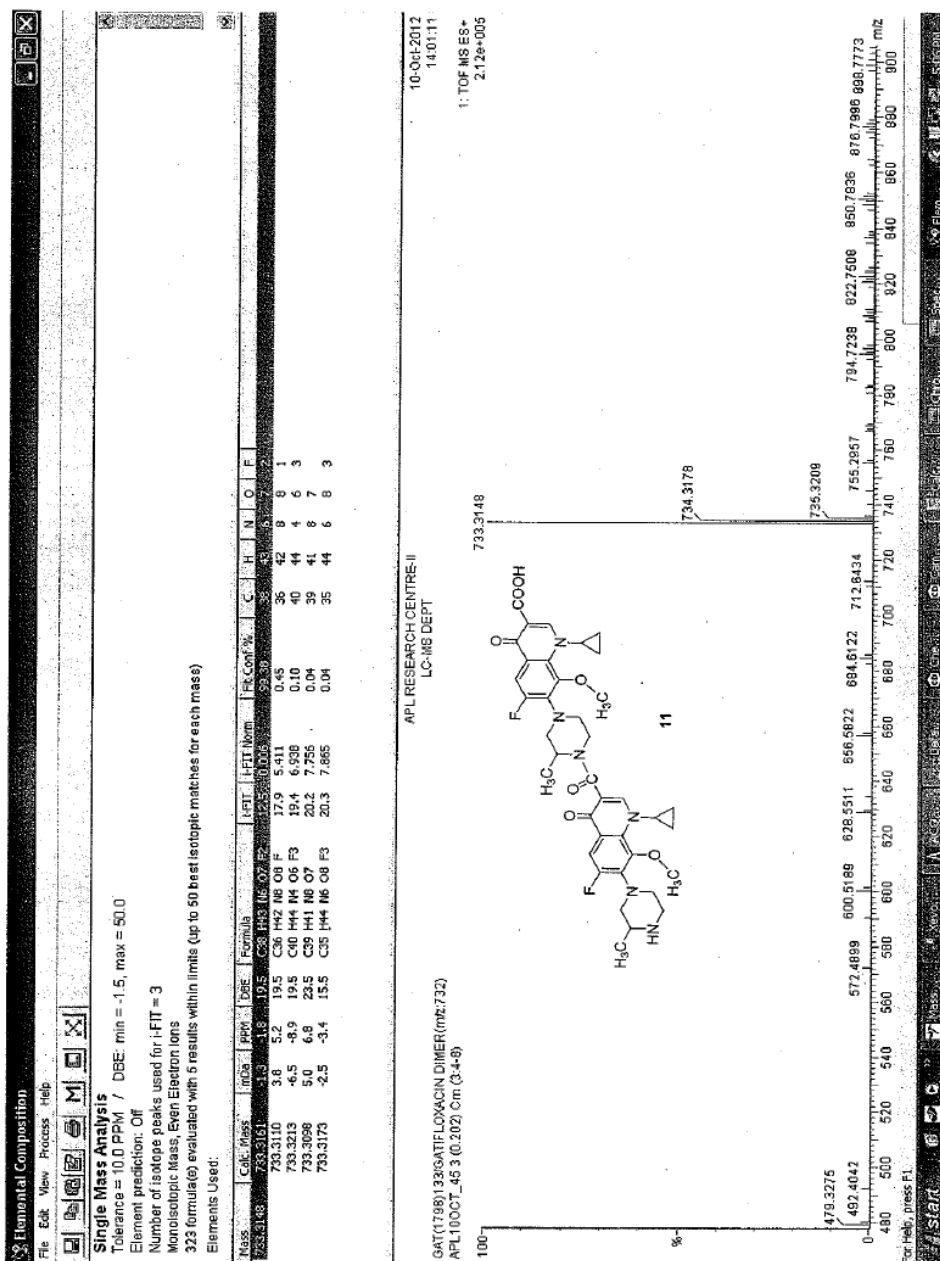
	RT (min)	Area (μV*sec)	% Area	Name
17	57.69	12467	0.11	Peak16
18	58.60	20639	0.19	Peak17

<sup>1</sup>H-NMR of Compound 11

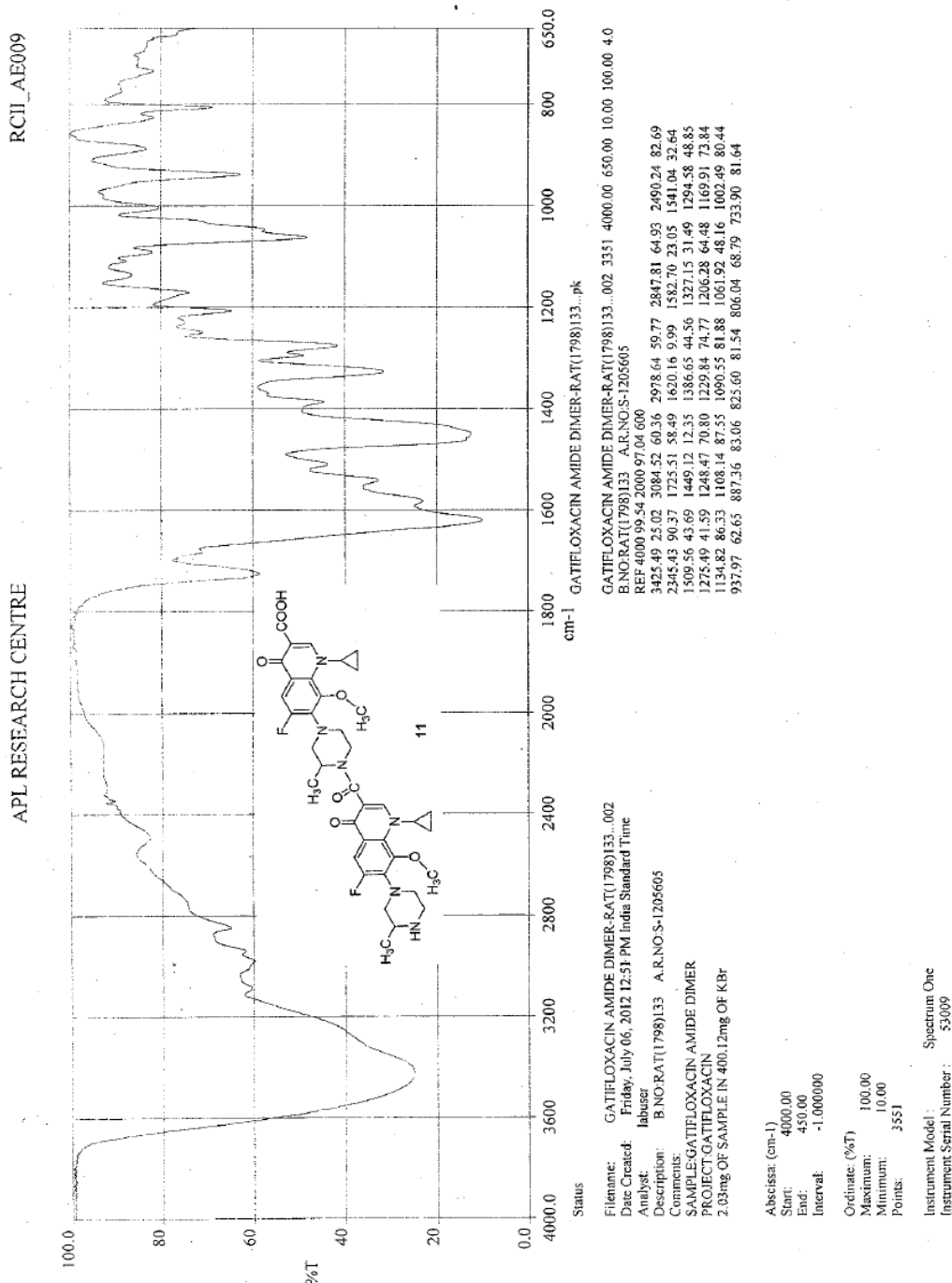


**<sup>13</sup>C-NMR of Compound 11**

# HRMS & Elemental analysis of Compound 11



**IR Spectrum of Compound 11**



**HPLC Purity of Compound 11**

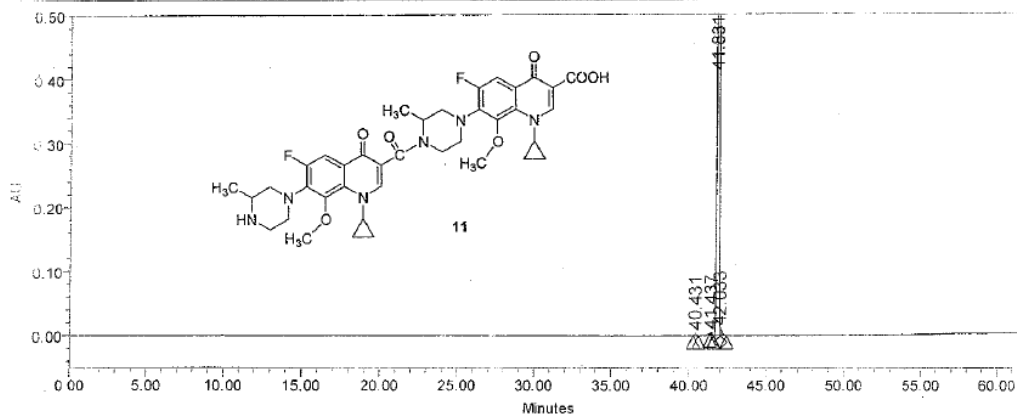
**APL RESEARCH CENTRE  
ANALYTICAL RESEARCH DEPARTMENT**

INSTRUMENT ID : RCII\_AE136

PROJECT NAME : SEP\_2012\RCII\_AE136

Sample ID : GAT(1798)133/Gatifloxacin  
Dimer(MZ=732)  
Run Time : 72.0 Minutes  
Vial : 5  
Injection : 1  
Injection Volume : 20.00 ul

Proc. Chnl. Descr : PDA 293.0 nm  
Date Acquired : 17/9/2012 17:48:13 IST  
Acq. Method Set : Gatifloxacin\_RS  
Date Processed : 18/9/2012 9:51:28 IST  
Processing Method : Gatifloxacin\_RS\_Pro



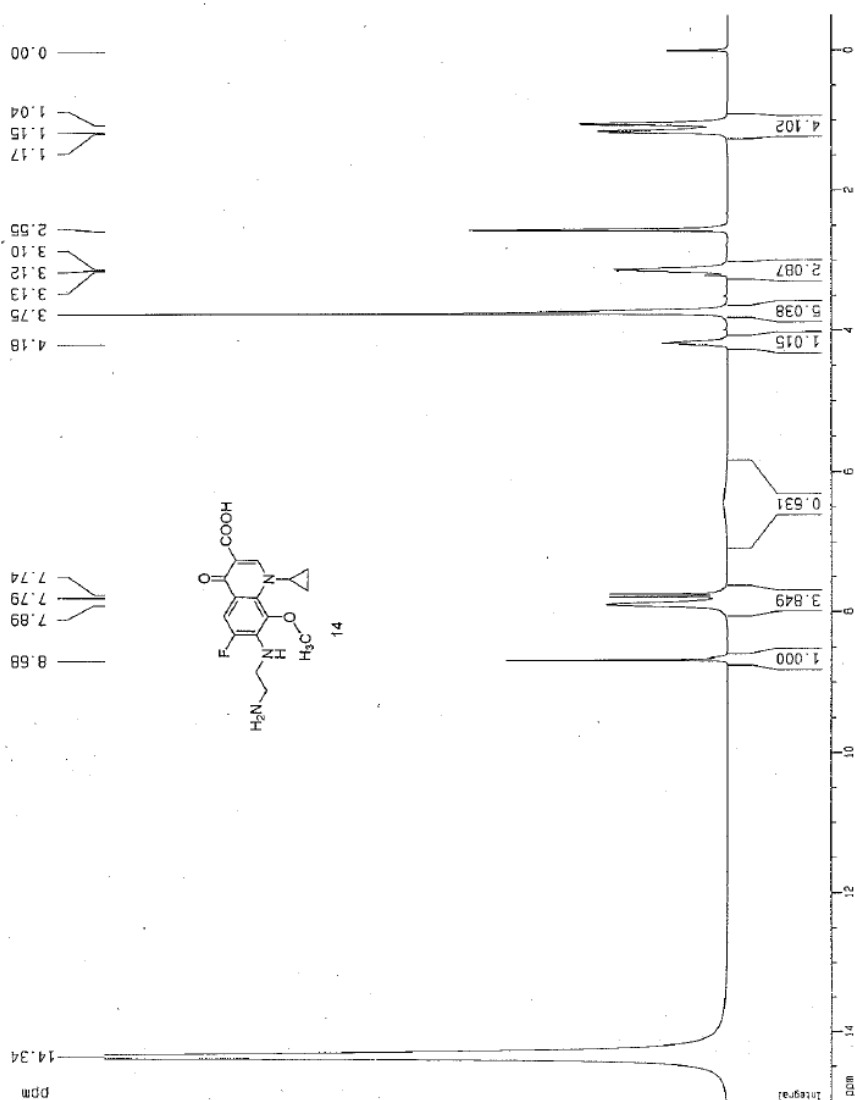
**Peak Results**

	RT (min)	Area (μV*sec)	% Area	Name
1	40.43	25985	0.12	Peak38
2	41.44	18527	0.09	Peak1
3	41.83	21379175	99.42	Peak39
4	42.03	80715	0.38	Peak40

<sup>1</sup>H-NMR of Compound 14

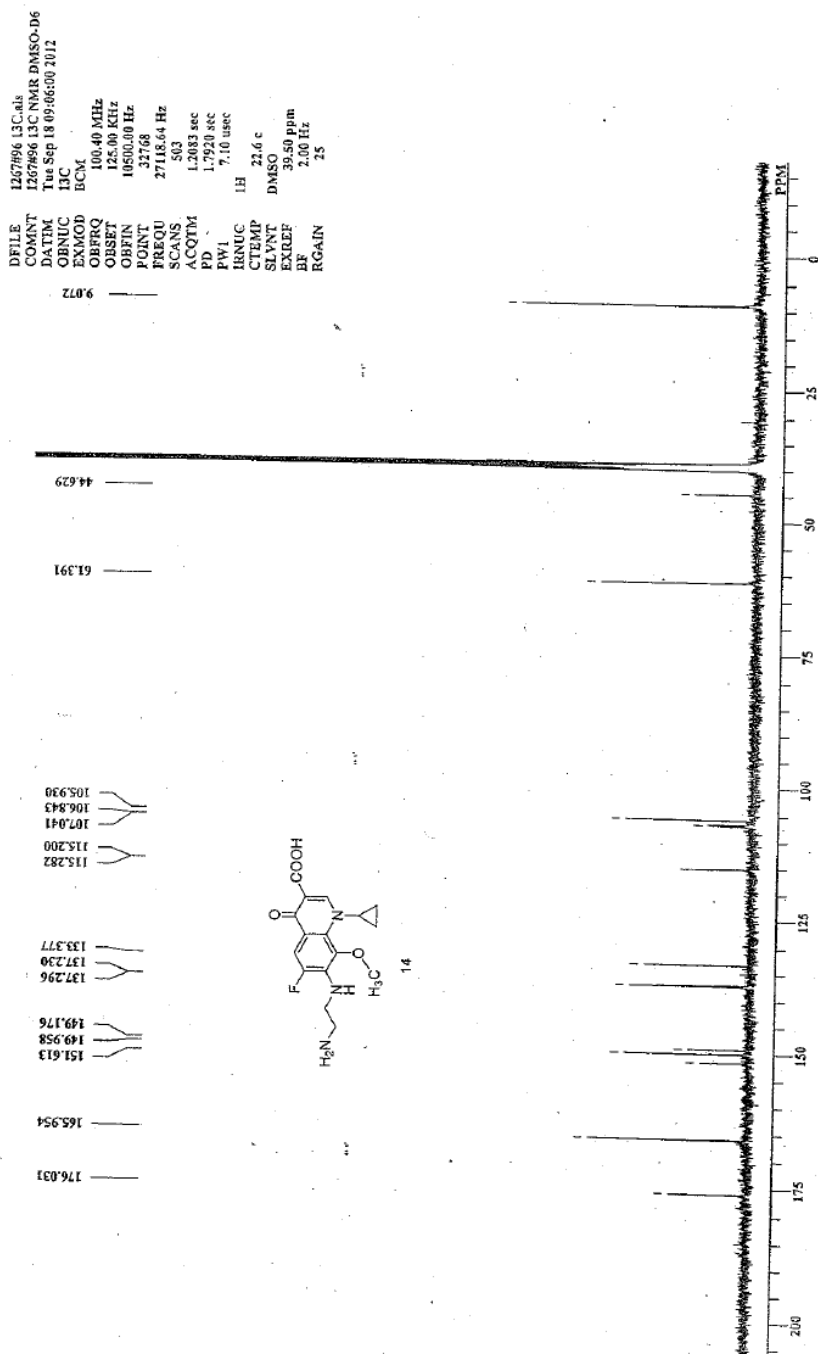
DIAMINO GATIFLOXACIN GAT (1267) 96 A. R. NO: S-0110  
DMSO-d6+1drop of TFA

APL-RESEARCH CENTRE  
Current Data Parameters  
NAME gat-1267-96  
EXPNO 2  
PROCNO 1  
F2 - Acquisition Parameters  
Date\_ 20110604  
Time 10.29  
INSTRUM dx300  
PROBHD 5 mm BBO BB-  
PULPROG zg30  
TD 32768  
RG 256  
SOLVENT DMSO  
NS 17  
AQ 1.8219508 sec  
DW 55.800 usec  
DE 6.00 usec  
D1 2.00000000 sec  
P1 6.75 usec  
PL1 -5.00 dB  
SFO1 300.1309366 MHz  
\*\*\*\*\* CHANNEL f1 \*\*\*\*\*  
NUC1 <sup>1</sup>H  
F2 - Processing parameters  
SI 32768  
SF 300.1299857 MHz  
WDW EN  
LB 0.30 Hz  
GB 0  
1D NMR plot parameters  
CX 20.50 cm  
F1P 15.000 ppm  
F2P -0.500 ppm

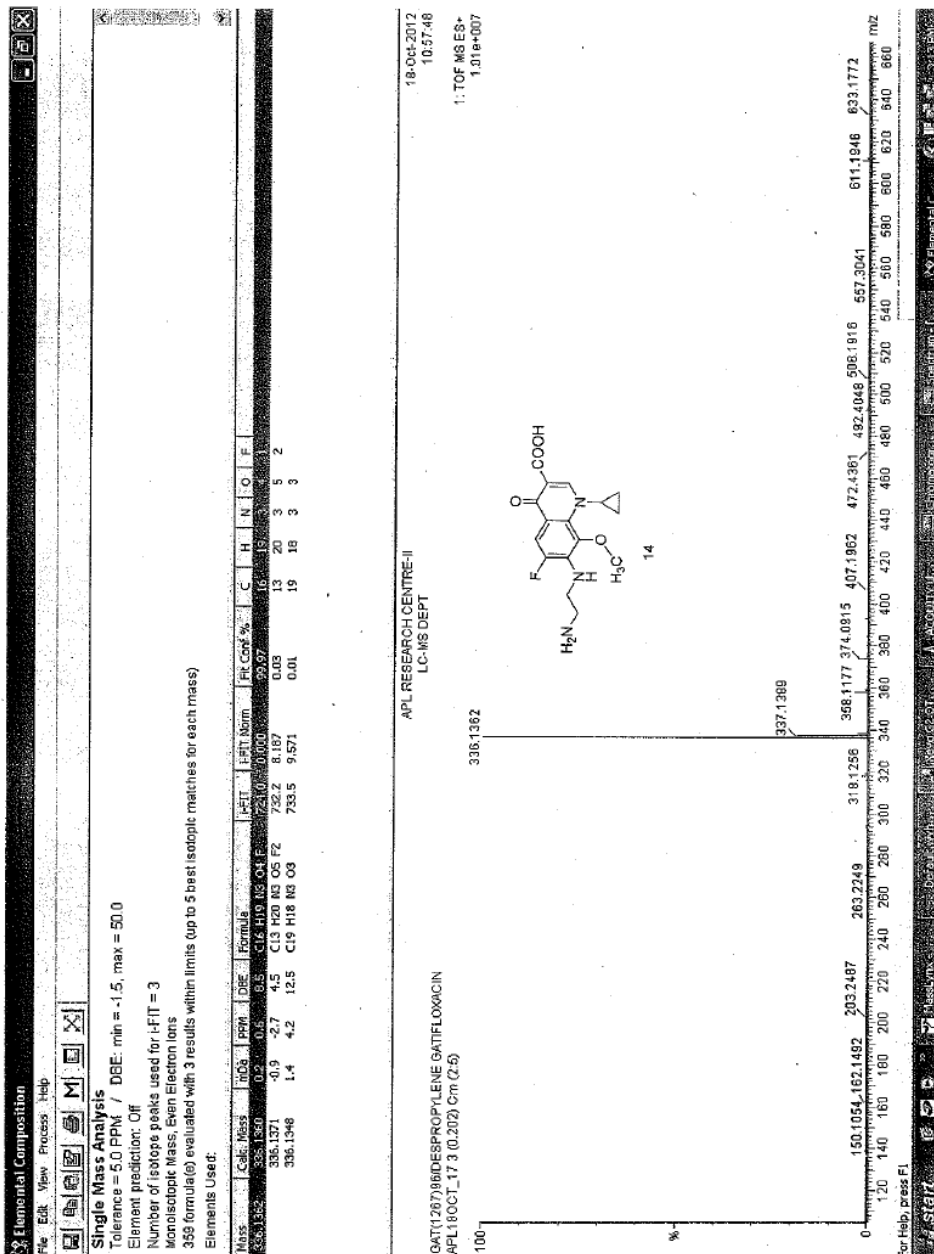




<sup>13</sup>C-NMR of Compound 14



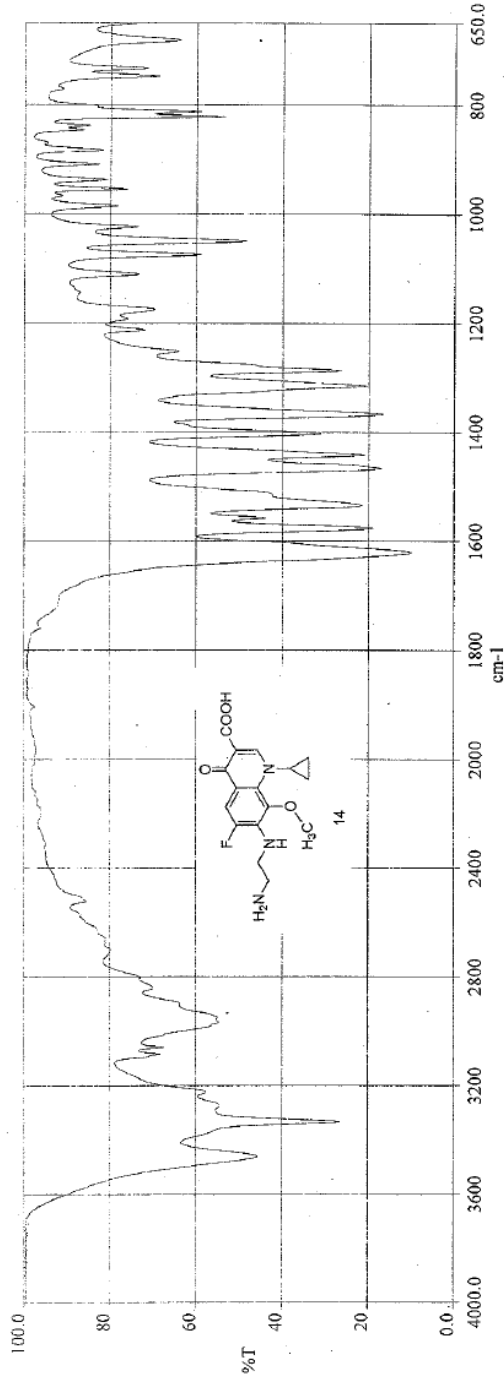
**HRMS & Elemental analysis of Compound 14**



IR Spectrum of Compound 14

RCIL\_AE009

APL RESEARCH CENTRE



Status

Filename: DIAMINO GATIFLOXACIN\_GAT(1267)96.002  
 Date Created: Friday, October 05, 2012 4:52 PM India Standard Time  
 Analyst: labuser  
 Description: B.NO:GAT(1267)96 A.R.NO.S-1208904  
 Comments:  
 SAMPLE:DIAMINO GATIFLOXACIN  
 PROJECT:GATIFLOXACIN  
 2.03mg SAMPLE IN 402.13mg KBr

Abscissa: (cm-1)  
 Start: 4000.00  
 End: 450.00  
 Interval: -1.000000

Ordinate: (%T)  
 Maximum: 100.00  
 Minimum: 10.00  
 Points: 3551

Instrument Model: Spectrum One  
 Instrument Serial Number: 42000

DIAMINO GATIFLOXACIN\_GAT(1267)96.pk  
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 B.NO:GAT(1267)96 A.R.NO.S-1208904  
 REF 4000 99.66 2000 97.41 600  
 3460.16 45.53 3332.06 26.23 3221.83 57.52 3083.66 68.21 3058.44 67.33  
 2967.47 54.47 2841.54 69.72 2701.88 79.75 2521.22 85.39 1983.09 97.09  
 1903.18 97.37 1620.54 9.96 1576.12 18.91 1557.77 43.79 1534.28 21.59  
 1466.41 17.04 1441.62 20.92 1402.04 31.16 1366.24 16.71 1314.28 20.37  
 1286.25 26.52 1251.13 63.98 1211.86 71.89 1191.72 75.88 1174.06 69.64  
 1109.80 73.13 1073.65 59.02 1048.93 48.45 1022.97 73.56 984.67 78.21  
 966.12 91.23 954.00 76.06 936.89 80.88 908.76 82.71 883.03 81.71  
 845.90 86.28 838.18 84.79 821.32 53.48 812.56 58.96 770.82 91.06  
 747.13 68.84 732.95 71.75 681.02 63.99

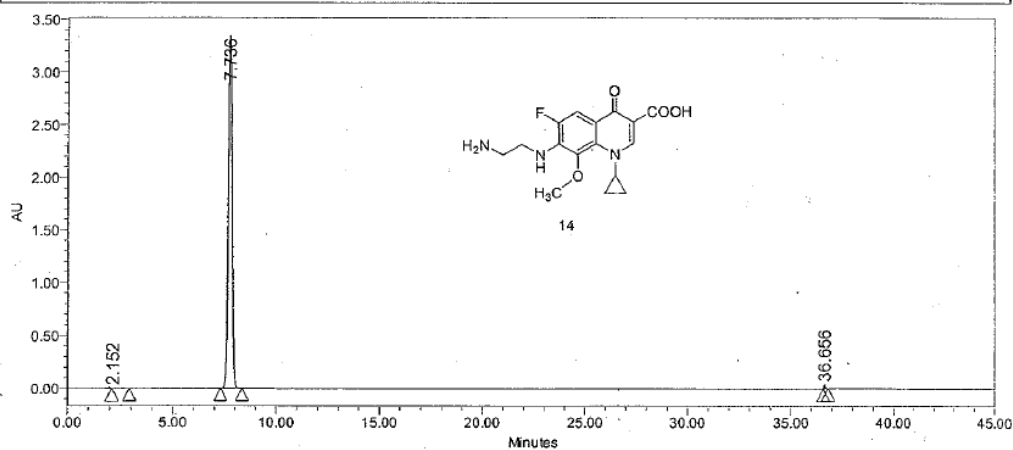
## HPLC Purity of Compound 14

### APL RESEARCH CENTRE ANALYTICAL RESEARCH DEPARTMENT

INSTRUMENT ID : ARE\_522\_PDA

PROJECT NAME : JUN\_2011\ARE\_522

Sample ID	: GAT(1267)96/ DiaminoGatifloxacin	Proc. Chnl. Descr	: PDA 293.0 nm
Run Time	: 55.0 Minutes	Date Acquired	: 6/3/2011 4:29:13 PM IST
Vial	: 29	Acq. Method Set	: Gatifloxacin_RS_METH
Injection	: 1	Date Processed	: 6/4/2011 9:28:15 AM IST
Injection Volume	: 20.00 ul	Processing Method	: Gatifloxacin_RS_PROC



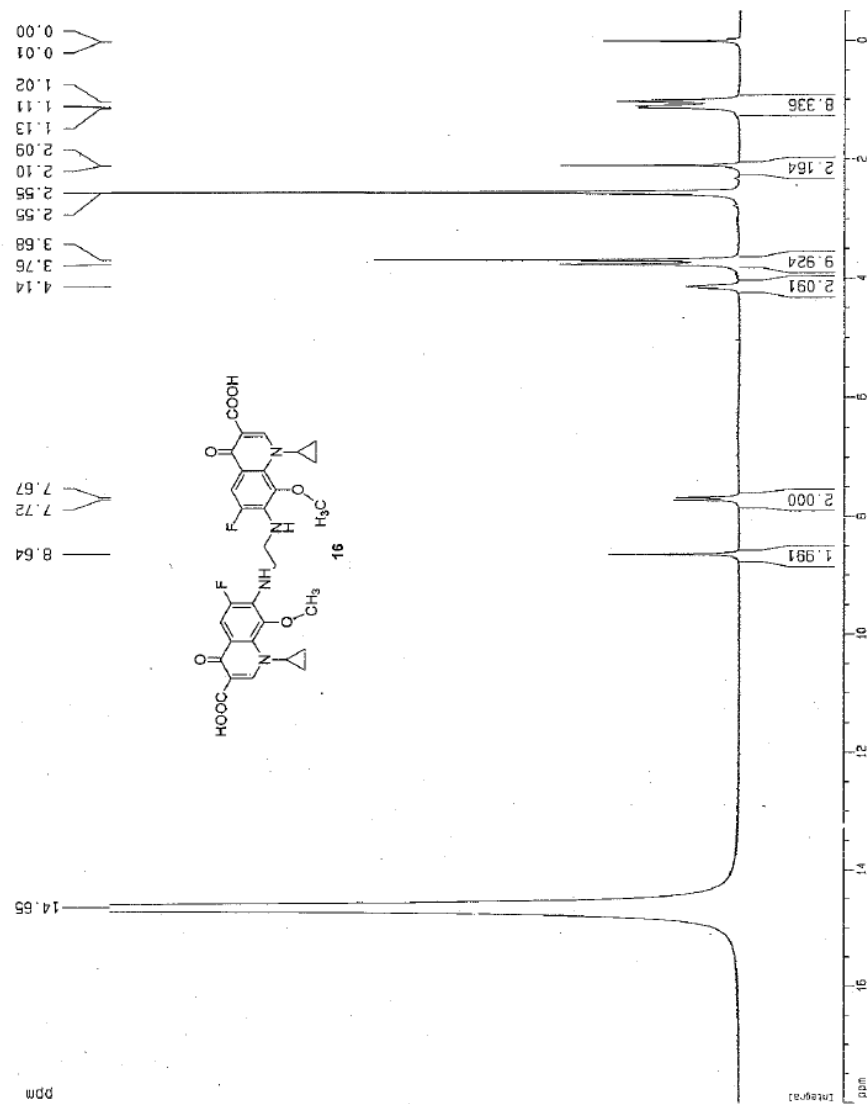
Peak Results

	RT (min)	Area ( $\mu\text{V}\cdot\text{sec}$ )	%Area	Name
1	2.15	24031	0.05	Peak1
2	7.706	45289002	99.84	Peak2
3	36.66	139549	0.31	Peak3

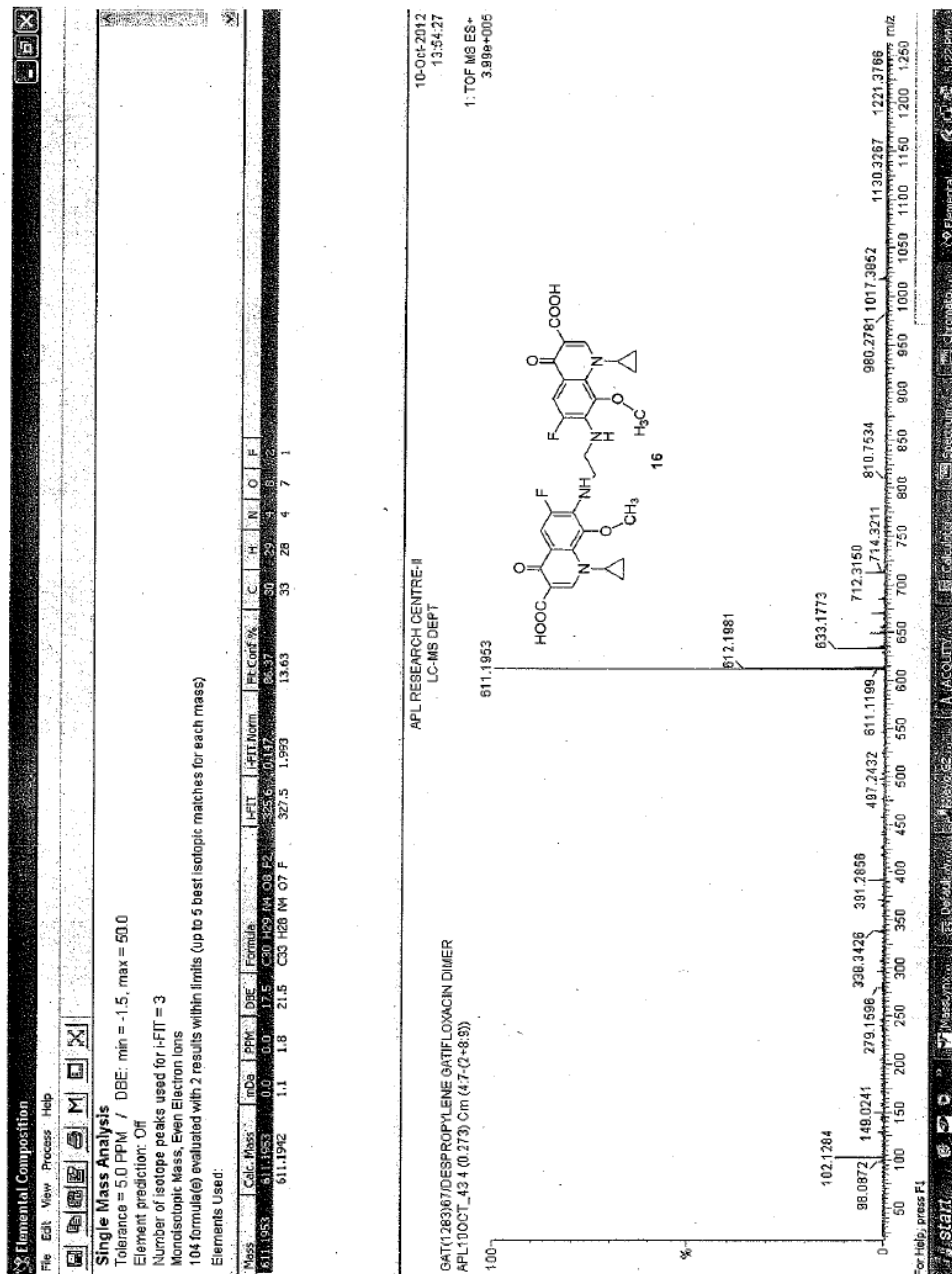
<sup>1</sup>H-NMR of Compound 16

DESOPROPYLENE GATIFLOXACIN DIMER GAT (1283) 67 A.R.NO: S-0110  
DMSO-d6+TFA

APL-RESEARCH CENTRE  
Current Data Parameters  
NAME gat-1283-67  
EXPNO 1  
PROCNO 1  
F2 - Acquisition Parameters  
Date\_ 20110708  
Time 15.48  
INSTRUM gdx300  
PROBHD 5 mm BBO BB-  
PULPROG zg30  
TD 32768  
RG 574.7  
SOLVENT DMSO  
NS 23  
AQ 1.8219508 sec  
DW 55.500 usec  
DE 5.00 usec  
D1 2.00000000 sec  
P1 6.75 usec  
PL1 -6.00 dB  
SFO1 300.1315006 MHz  
\*\*\*\*\* CHANNEL f1 \*\*\*\*\*  
NUC1 <sup>1</sup>H  
F2 - Processing parameters  
SI 32768  
SF 300.1299874 MHz  
WDW EM  
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GB 0  
1D NMR plot parameters  
CX 20.50 cm  
F1P 16.000 ppm  
F2P -0.500 ppm



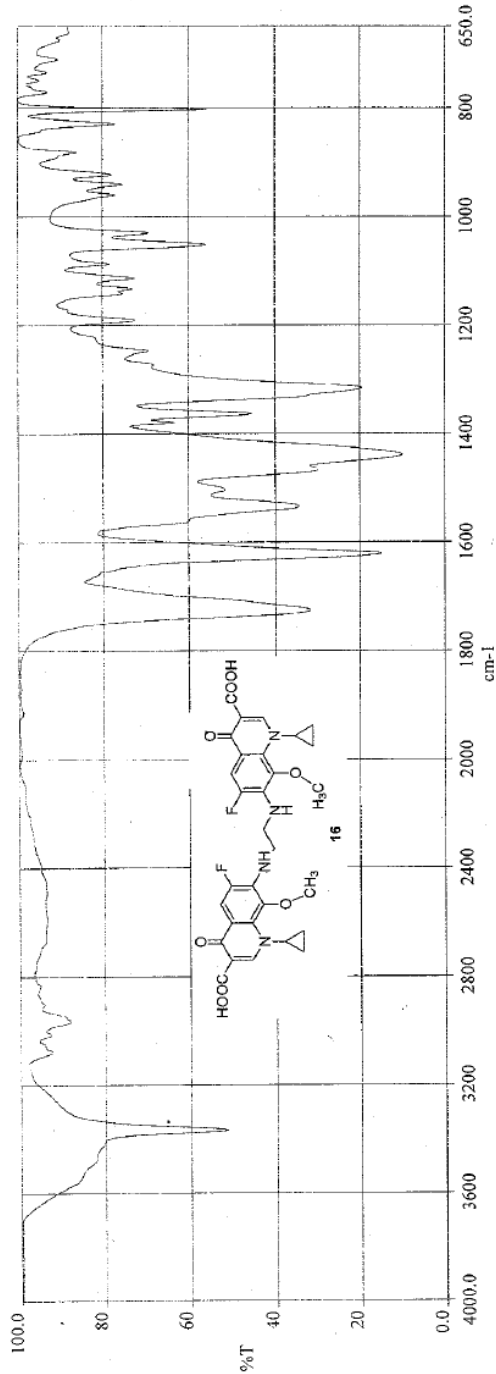
## HRMS &amp; Elemental analysis of Compound 16



IR Spectrum of Compound 16

RCIL\_AE009

APL RESEARCH CENTRE



Status

Filename: DESPROPYLENE GATIFLOXACIN DIMER-GAT(1283)67.002  
 Date Created: Friday, July 06, 2012 1:05 PM India Standard Time  
 Analyst: labuser  
 Description: B.NO:GAT(1283)67 A.R.NO:S-1205605  
 Comments:  
 SAMPLE: DESPROPYLENE GATIFLOXACIN DIMER  
 PROJECT: GATIFLOXACIN  
 2.04mg OF SAMPLE IN 400.16mg OF KBr

DESPROPYLENE GATIFLOXACIN DIMER-GAT(1283)67.pk

DESPROPYLENE GATIFLOXACIN DIMER-GAT(1283)67.002 3351 4000.00 650.00 10.00 10  
 B.NO:GAT(1283)67 A.R.NO:S-1205605  
 REF: 4000.99 82.2000 99.54.600  
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 1725.28 31.76 1620.81 14.80 1535.25 34.33 1503.80 51.54 1465.94 29.90  
 1438.94 9.99 1378.66 63.14 1363.10 45.34 1314.76 19.54 1246.48 69.04  
 1190.05 72.45 1132.15 72.85 1112.91 72.36 1086.49 78.43 1050.91 55.92  
 1029.17 69.12 959.58 76.92 940.39 75.25 922.88 77.80 882.04 85.94  
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 710.47 90.40

Abscissa: (cm-1)  
 Start: 4000.00  
 End: 450.00  
 Interval: -1.000000

Ordinate: (%T)  
 Maximum: 100.00  
 Minimum: 10.00  
 Points: 3551

Instrument Model: Spectrum One

6/12/12  
 CS4

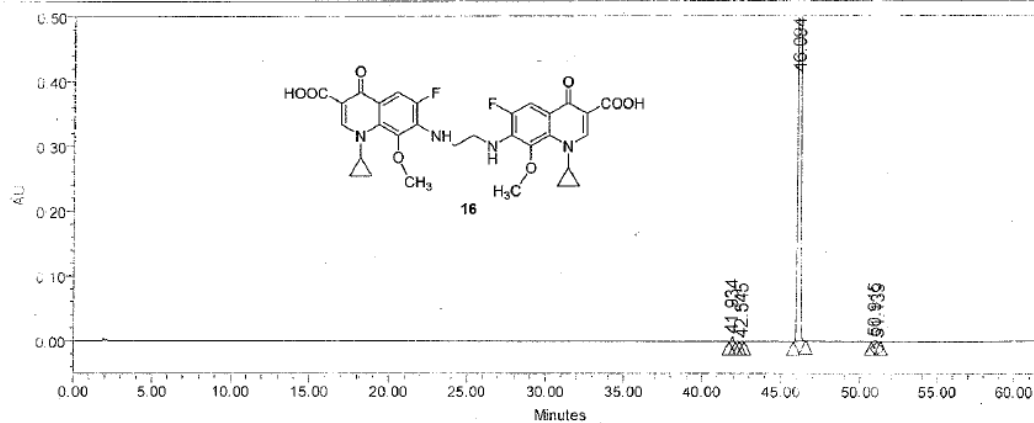
## HPLC Purity of Compound 16

APL RESEARCH CENTRE  
ANALYTICAL RESEARCH DEPARTMENT

INSTRUMENT ID: RCIL\_AE136

PROJECT NAME: SEP\_2012\RCIL\_AE136

Sample ID	GAT(1283)67/Gatifloxacin Dimer(MZ=610)	Proc. Chnl. Descr	PDA 293.0 nm
Run Time	72.0 Minutes	Date Acquired	17/9/2012 16:34:56 IST
Vial	4	Acq. Method Set	Gatifloxacin_RS
Injection	1	Date Processed	18/9/2012 10:11:24 IST
Injection Volume	20.00 ul	Processing Method	Gatifloxacin_RS_Pro



Peak Results

	RT (min)	Area ( $\mu\text{V}\cdot\text{sec}$ )	% Area	Name
1	41.93	46546	0.30	Peak2
2	42.55	7278	0.05	Peak4
3	46.09	15378098	99.45	Peak5
4	50.92	22885	0.15	Peak7
5	51.14	7595	0.05	Peak8



**Impurity mixture of dimers**

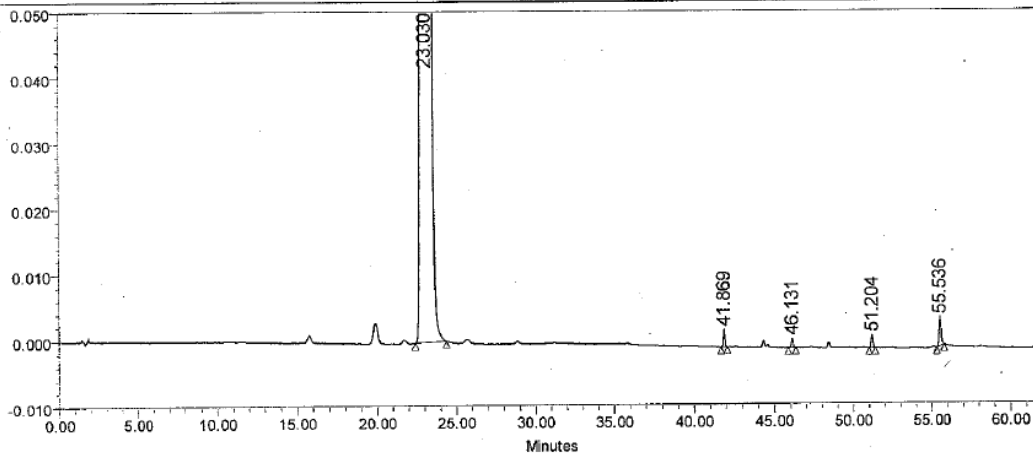
**APL RESEARCH CENTRE-II  
ANALYTICAL RESEARCH DEPARTMENT**

INSTRUMENT ID RCI\_AE136

PROJECT NAME SEP\_2012\RCI\_AE136

Sample ID: Gatifloxacin Dimers Impurity Mix  
 vial: 9  
 Injection: 1  
 Injection Volume: 20.00 ul  
 Run Time: 72.0 Minutes

Proc. Chnl. Descr.: PDA 293.0 nm  
 Date Acquired: 9/18/2012 12:34:14 PM IST  
 Acq. Method Set: Gatifloxacin\_RS  
 Date Processed: 9/18/2012 1:48:41 PM IST  
 Processing Method: Gatifloxacin\_RS\_Pro



**PEAK RESULTS**

	RT	USP Plate Count	USP Tailing	USP Resolution	RT Ratio	Name
1	23.03	23268	1.31			Gatifloxacin
2	41.87	783805	1.03	46.66	1.82	Gatifloxacin Dimer (M/Z=732)
3	46.13	661209	0.97	20.15	2.00	Gatifloxacin Dimer (M/Z=610)
4	51.20	743010	1.00	21.51	2.22	Gatifloxacin Dimer (M/Z=652)
5	55.54	884483	1.06	17.88	2.41	Gatifloxacin Dimer (M/Z=650)