Chapter 8

References

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Appendix

LD_{50} of *N-benzyl piperazinyl sulfonamide derivatives*

LD_{50} determination of compound 72

Table A0.1 LD_{50} determination protocol for compound **72**

Test substance 1. Physical nature 2. Code	 Solid 72
Vehicle	0.5% CMC solution in water
Test animals 1. Sex 2. Number	Rat Female 3
Test conditions 1. Dose 2. Rationale for the selection of the starting dose 3. Dosing volumes 4. Time & date of dosing	 300 mg/kg 0.7 ml 12:30 pm 14/01/2023

Table T3 Effect of compound **72** on the body wt. of the animals at the dose of 300 mg/kg.

Group	**Body wt. (gm) on 14/01/2023 at 12:20 pm**	**Body wt. (gm) on 15/01/2023 at 12:20 pm**	**Body wt. (gm) on 16/01/2023 at 12:20 pm**	**Body wt. (gm) on 17/01/2023 at 12:20 pm**	**Body wt. (gm) on 18/01/2023 at 12:20 pm**
1	215	214	207	217	228
2	228	223	230	239	244
3	235	234	225	238	247

Table T4 The onset of toxicity with compound **72** in the period of 72h.

Group	**Body wt. Changes (gm)**					**Onset of toxicity**	**Reversibility**	**Date & time of death**
	14/1/23	**15/1/23**	**16/1/23**	**17/01/23**	**18/01/23**			
1	00	02	01	4	5	-	-	-
2	00	01	01	4	6	-	-	-
3	00	02	03	5	10	-	-	-

Discussion and interpretation of results: Animals were dosed as per the OECD guideline 423 at 300 mg/kg doses. All animals were alive at 300mg/kg dose within 72 hrs and next 14 days.

Conclusions: No toxicity was observed at **300mg/kg**.

Table A0.2 LD_{50} determination protocol for the compound **72**.

Test substance 1. Physical nature 2. Code	 Solid **72**
Vehicle	0.5% CMC solution in water
Test animals 1. Sex 2. Number	Rat Female 3
Test conditions 1. Dose 2. Rationale for the selection of the starting dose 3. Dosing volumes 4. Time & date of dosing	 2000 mg/kg No death at 300mg/kg 0.7 ml 11:15 pm 19/01/2023

Table A0.3 Effect of compound **72** on the body wt. of the animals at the dose of 2000 mg/kg.

Group	Body wt. (gm) on 19/01/2023at 11 am	Body wt. (gm) on 20/01/2023 at 11 am	Body wt. (gm) on 21/01/2023 at 11 am
1	220	-	-
2	211	-	-
3	236	-	-

Table A0.4 The onset of toxicity with compound **72** in the period of 72h.

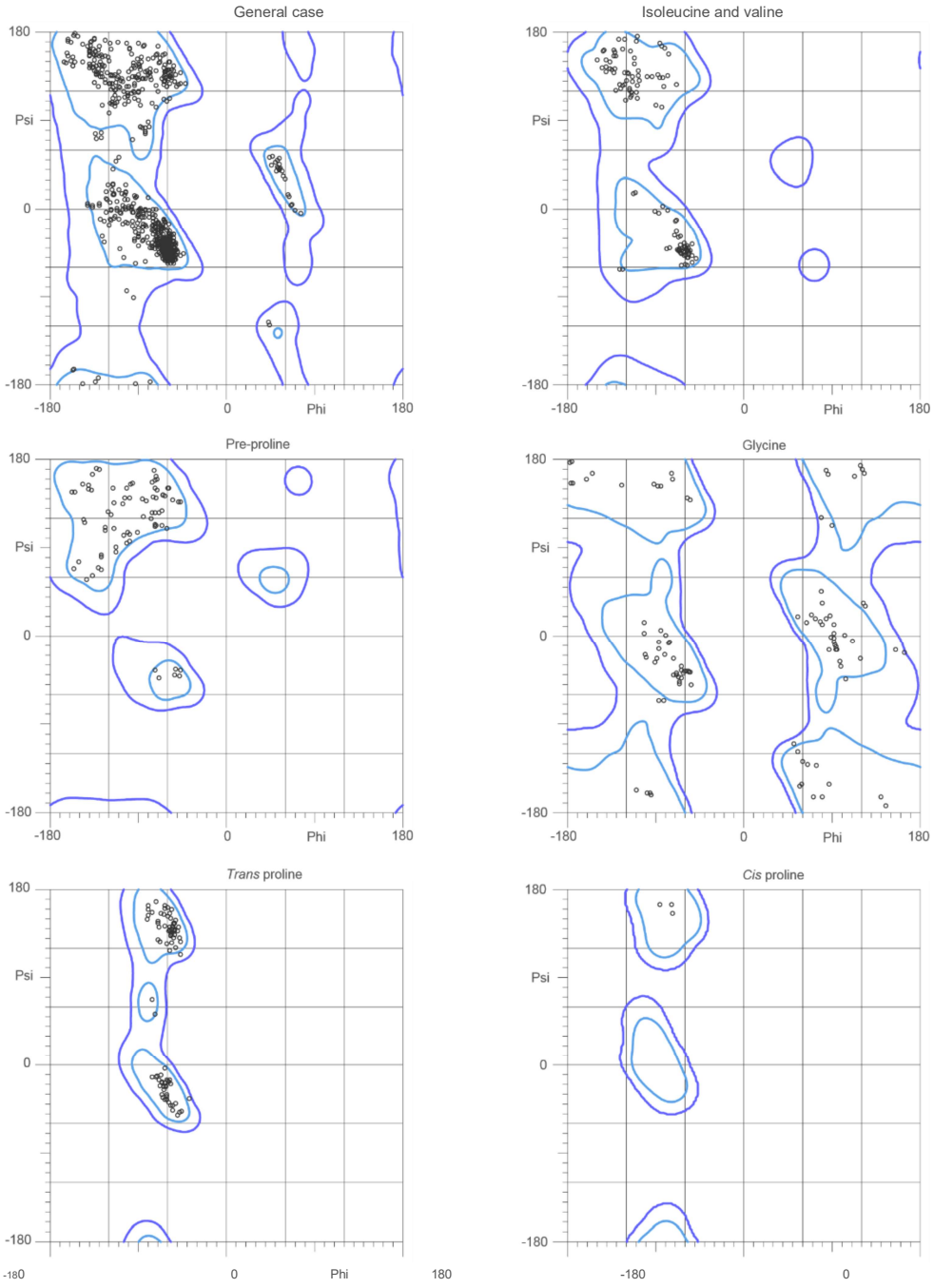
Group	Body wt. Changes (gm)			Onset of toxicity	Reversibility	Date & time of death
	19/01/23	20/01/23	21/01/23			
1	0	0	0	19/01/23, 3:30 pm	No	19/01/23, 7:43 pm
2	0	0	0	19/01/23, 3:50 pm	No	19/01/23, 6 pm
3	0	0	0	-	No	20/01/23, 8:30 am

Discussion and interpretation of results: Animals were dosed as per the OECD guideline 423 at 300 mg/kg and 2000 mg/kg doses. All animals died at 2000 mg/kg dose within 72 hrs.

Conclusions: As per OECD guideline **LD_{50} = 1000 mg/kg**.

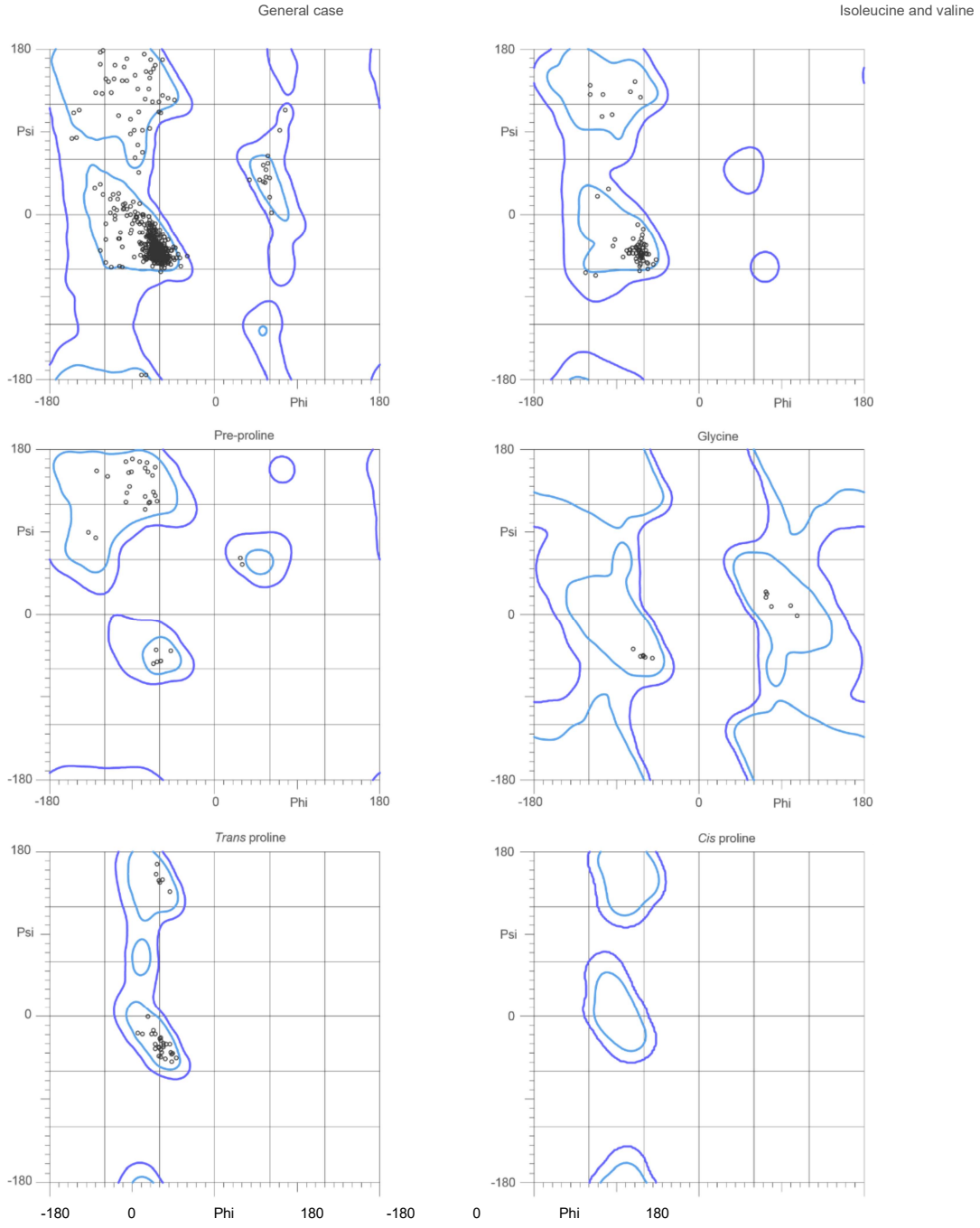
MolProbity Ramachandran analysis

4ey7.pdb, model 1



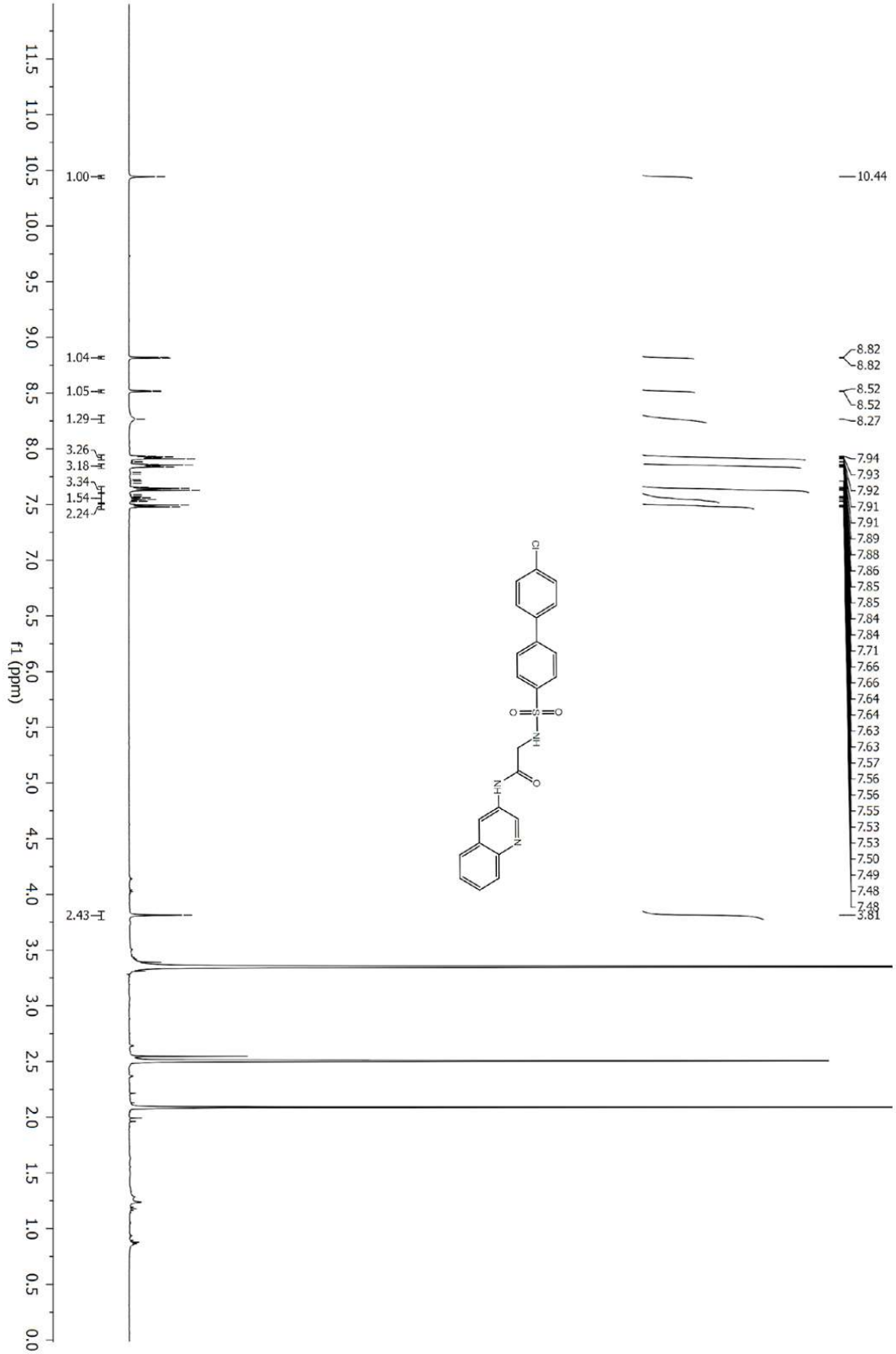
97.1% (1040/1071) of all residues were in favored (98%) regions.
100.0% (1071/1071) of all residues were in allowed (>99.8%) regions.
There were no outliers
Lovell, Davis, et al. Proteins 50:437 (2003)

MolProbity Ramachandran analysis
6a3n.pdb, model 1



6.6% (618/640) of all residues were in favored (98%) regions.
100.0% (640/640) of all residues were in allowed (>99.8%) regions.
There were no outliers.
Lovell, Davis, et al. Proteins 50:437 (2003)

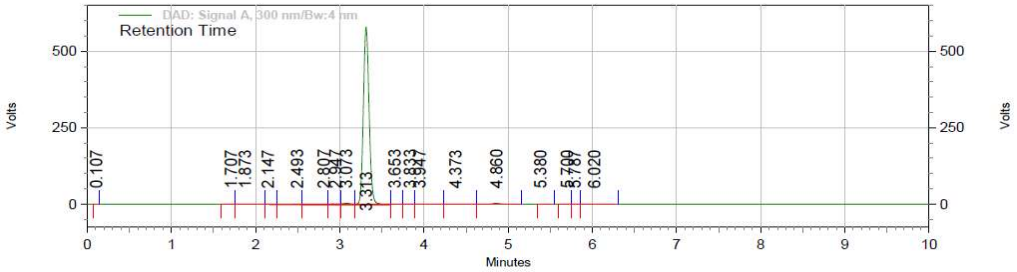
^{1}H NMR of Compound 41



HPLC data of Compound 41

Area % Report

Data File: C:\DATA\SKSINGH\RAYALA\COMPOUND-41 152018-11-03 12-02-33 (GMT +05-30).rslt\COMPOUND-41-125.dat
Method: C:\Enterprise\Projects\Method\untitled.met
Acquired: 03-11-2018 12:15:47 (GMT +05:30)
Printed: 03-11-2018 12:52:10 (GMT +05:30)



DAD: Signal A, 300 nm/Bw:4 nm Results

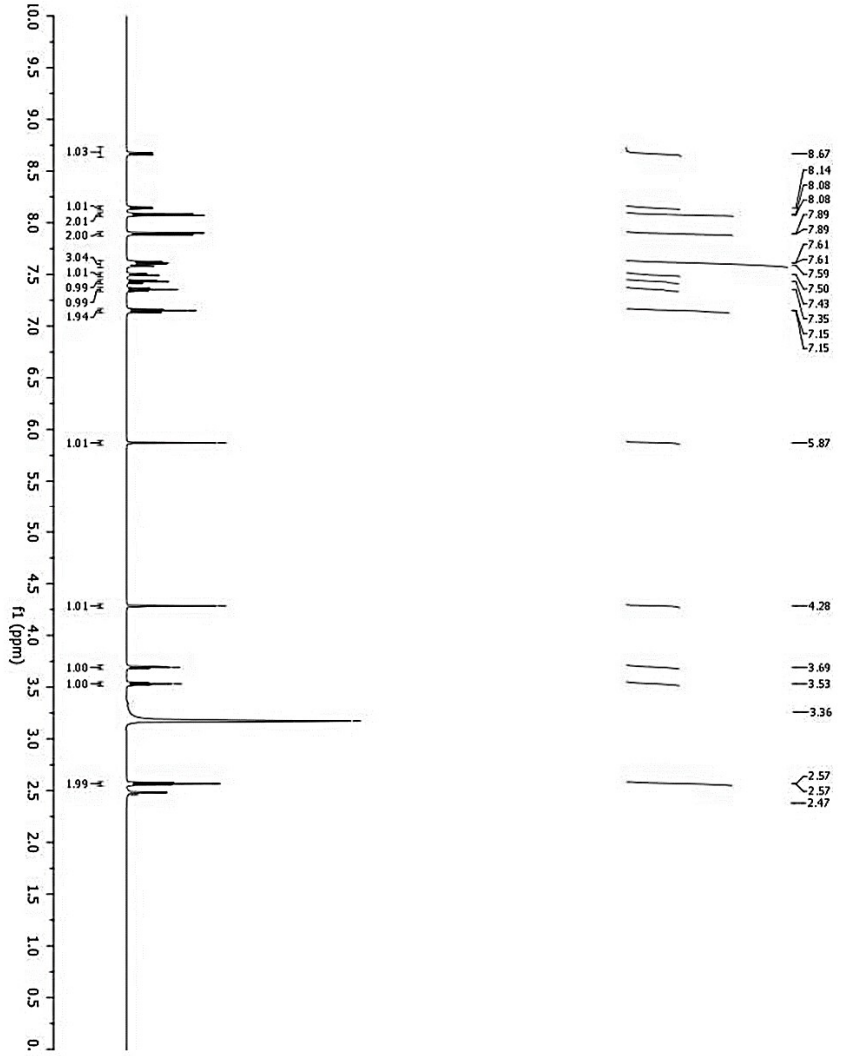
Retention Time	Area	Area %	Height	Height %
0.107	48	0.00	20	0.00
1.707	2078	0.03	288	0.02
1.873	17681	0.29	780	0.06
2.147	10536	0.17	1196	0.10
2.493	33574	0.56	3592	0.29
2.807	33708	0.56	2311	0.19
2.947	28803	0.48	4516	0.36
3.073	39684	0.66	5587	0.45
3.313	5743115	95.39	1215865	97.56
3.653	15574	0.26	2111	0.17
3.833	15512	0.26	2162	0.17
3.947	27921	0.46	2355	0.19
4.373	15979	0.27	770	0.06
4.860	35263	0.59	4570	0.37
5.380	153	0.00	14	0.00
5.700	156	0.00	29	0.00
5.787	106	0.00	25	0.00
6.020	1053	0.02	101	0.01
Totals	6020944	100.00	1246292	100.00

Retention Time	Area	Area %	Height	Height %
3.313	6087249	99.01	1227953	99.60
4.860	54922	0.89	4916	0.40
6.900	6164	0.10	63	0.01
Totals	6148335	100.00	1232932	100.00

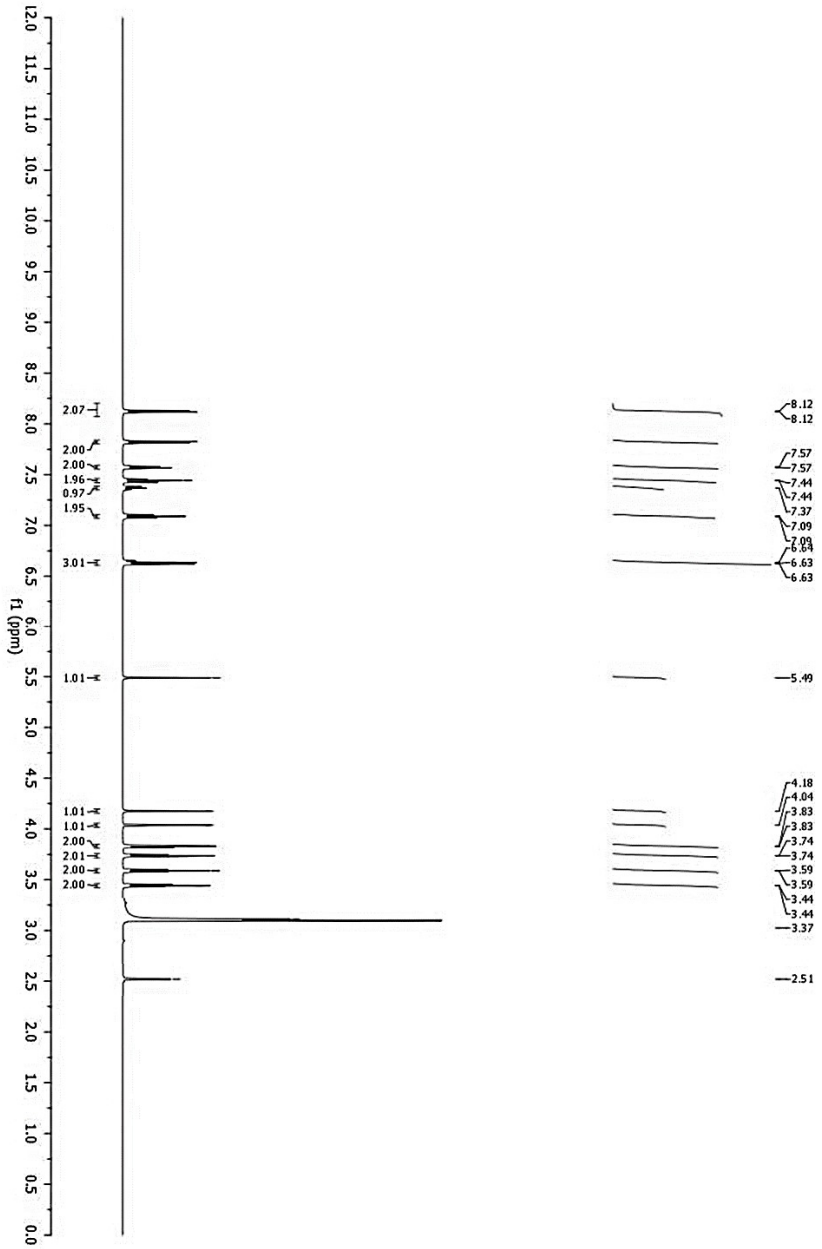
215.0 nm Results

Retention Time	Area	Area %	Height	Height %

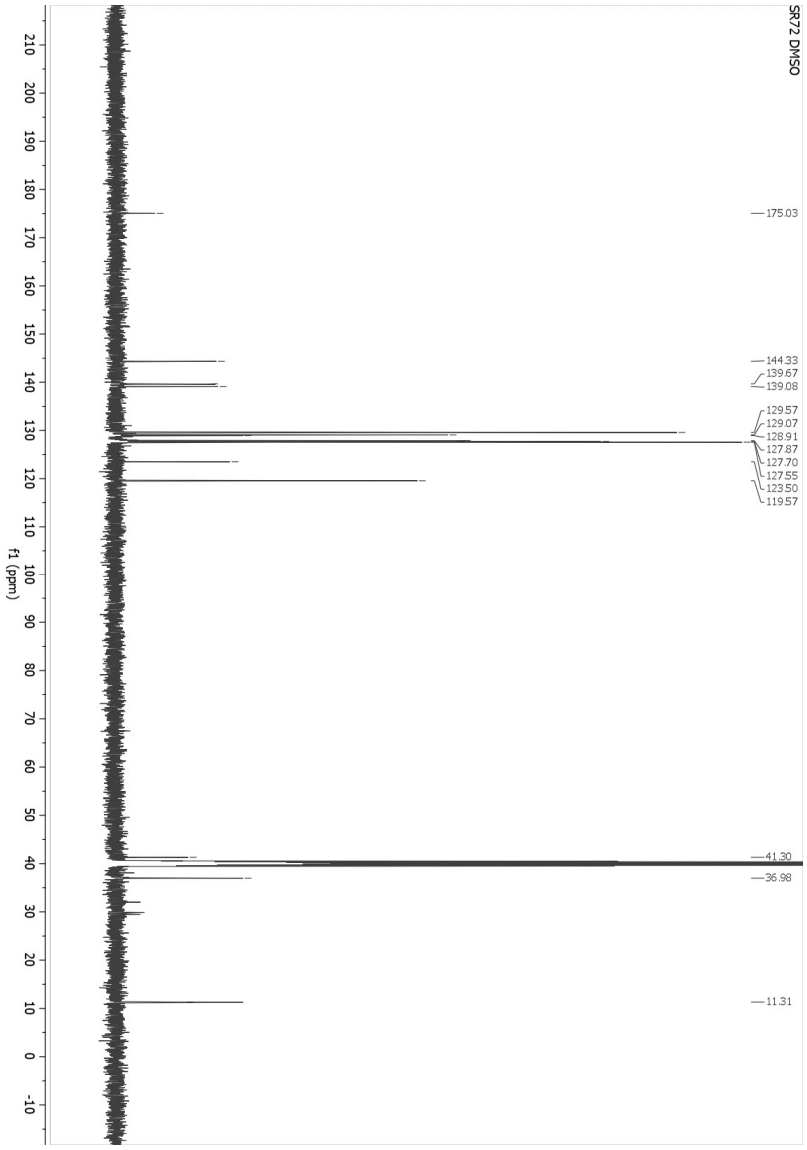
^{1}H NMR of Compound 42



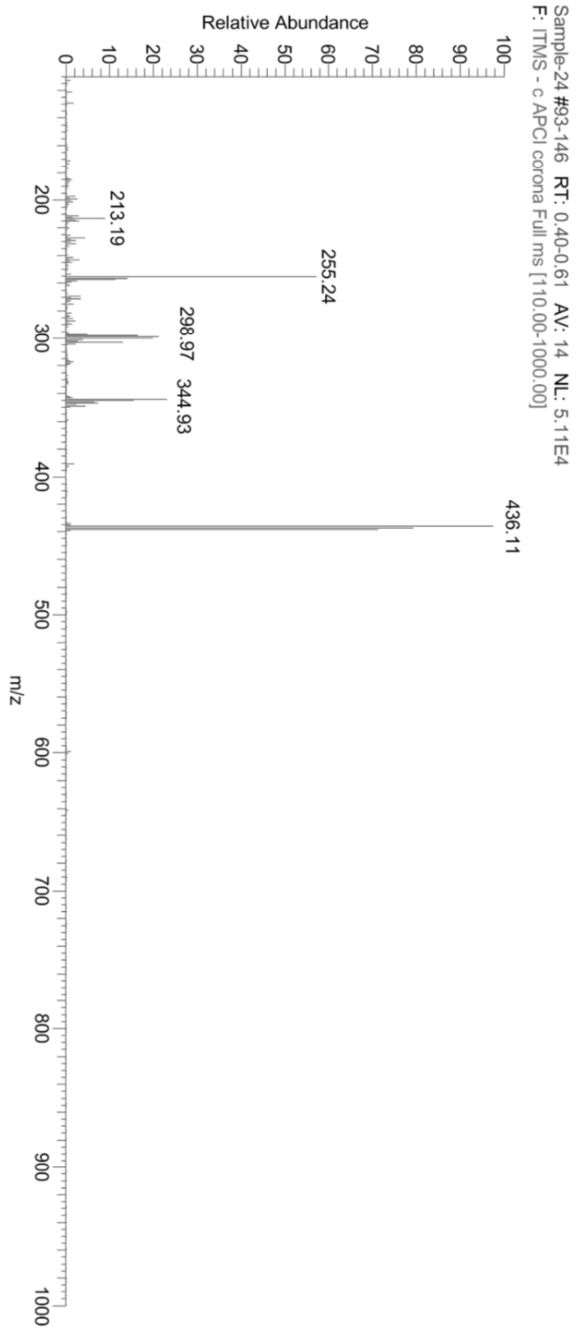
^{1}H NMR of Compound 72



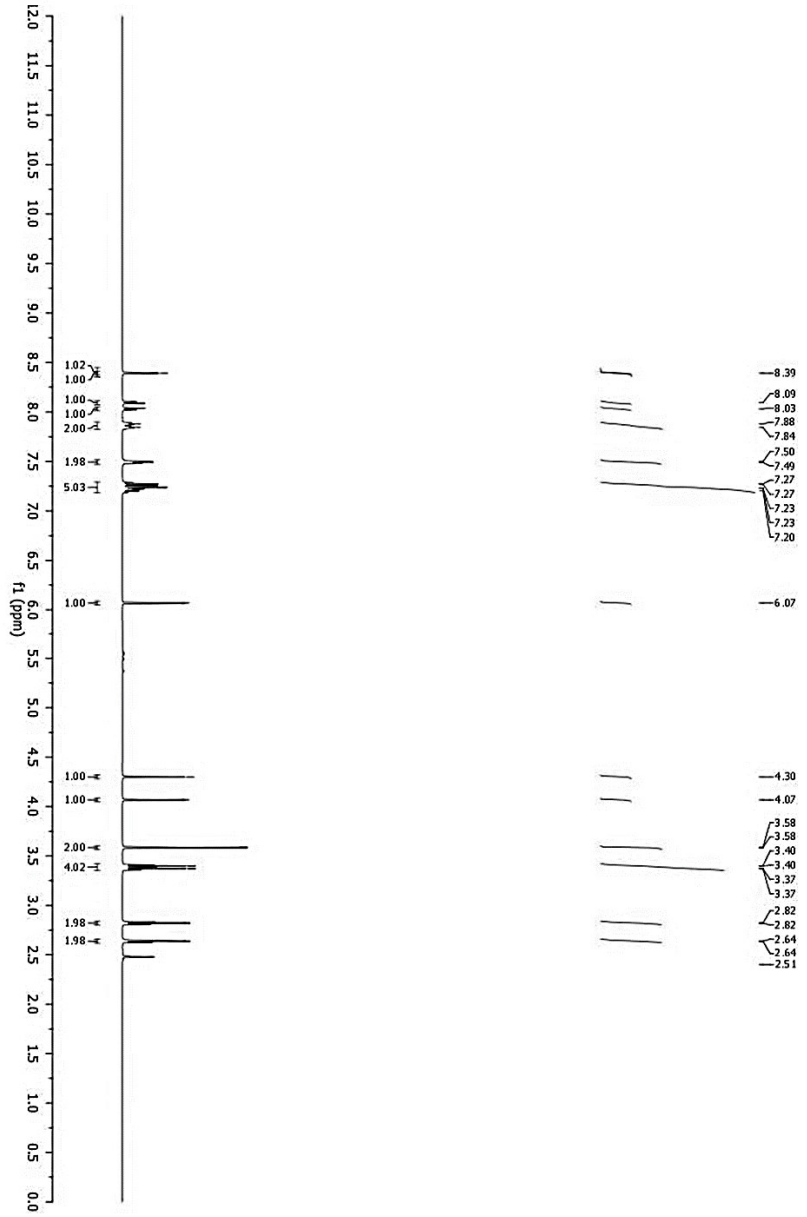
^{13}C NMR of Compound 72



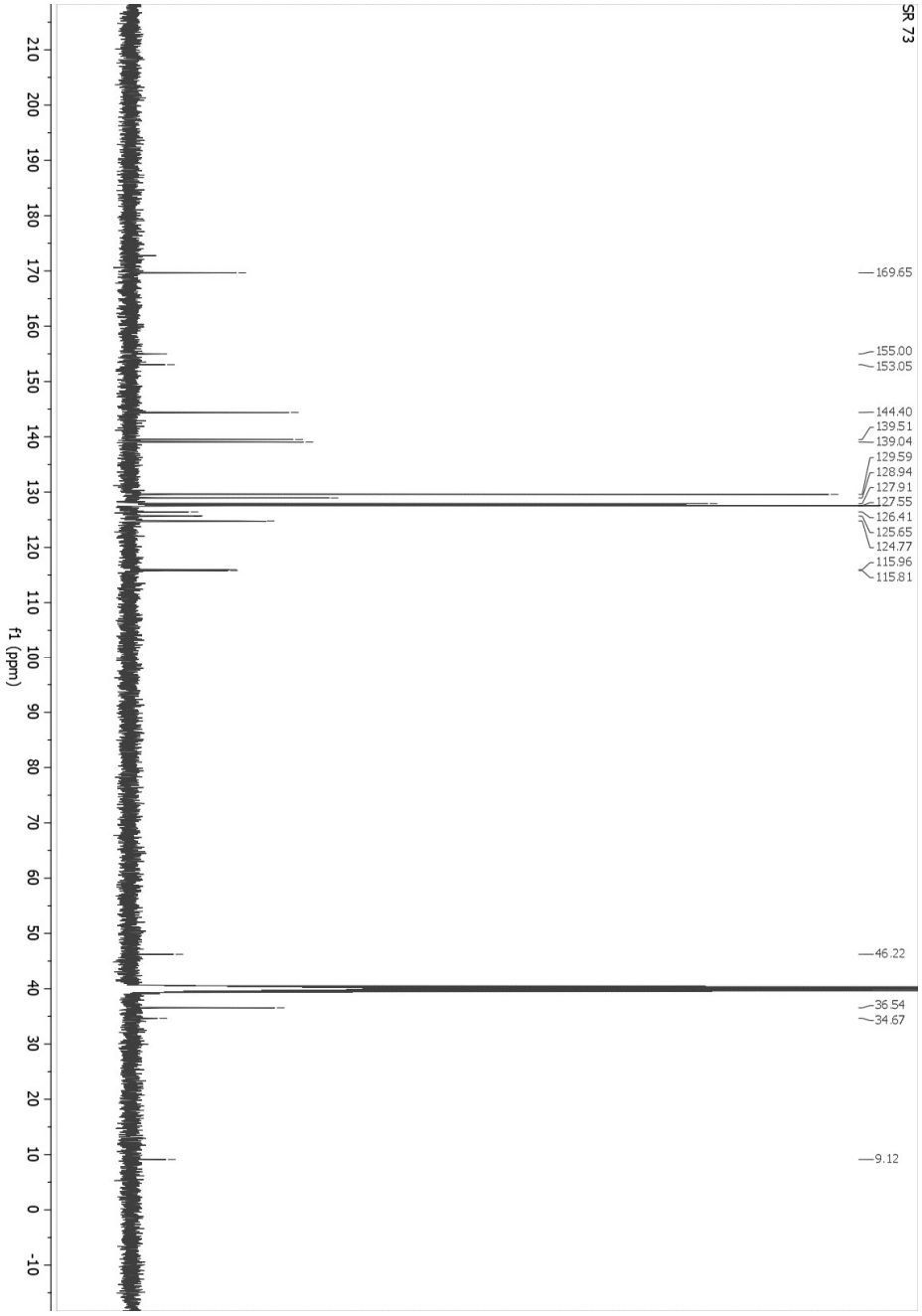
LCMS of Compound 72



^{1}H NMR of Compound 73



^{13}C NMR of Compound 73



List of Publications

1. Rayala Swetha, Anjali Sharma, Ravi Singh, Ankit Ganeshpurkar, Devendra Kumar, Ashok Kumar, and Sushil K. Singh. "Combined ligand-based and structure-based design of PDE 9A inhibitors against Alzheimer's disease." Molecular Diversity 26, no. 5 (2022): 2877-2892.
2. Rayala Swetha, Chandrim Gayen, Devendra Kumar, Tryambak Deo Singh, Gyan Modi, and Sushil Kumar Singh. "Biomolecular basis of matrix metallo proteinase-9 activity." Future medicinal chemistry 10, no. 9 (2018): 1093-1112.
3. Rayala Swetha, Devendra Kumar, Sukesh K. Gupta, Ankit Ganeshpurkar, Ravi Singh, Gopichand Gutti, Dileep Kumar, Srabanti Jana, Sairam Krishnamurthy, and Sushil K. Singh. "Multifunctional hybrid sulfonamides as novel therapeutic agents for Alzheimer's disease." Future Medicinal Chemistry 11, no. 24 (2019): 3161-3178.
4. Ghosh, Powsali, Ravi Singh, Ankit Ganeshpurkar, Rayala Swetha, Devendra Kumar, Sushil Kumar Singh, and Ashok Kumar. "Identification of potential death-associated protein kinase-1 (DAPK1) inhibitors by an integrated ligand-based and structure-based computational drug design approach." Journal of Biomolecular Structure and Dynamics (2022): 1-13.
5. Singh, Ravi, Ankit Vyankatrao Pokle, Powsali Ghosh, Ankit Ganeshpurkar, Rayala Swetha, Sushil Kumar Singh, and Ashok Kumar. "Pharmacophore-based virtual screening, molecular docking and molecular dynamics simulations study for the identification of LIM kinase-1 inhibitors." Journal of Biomolecular Structure and Dynamics (2022): 1-15.
6. Bajad, Nilesh Gajanan, Rayala Swetha, Ravi Singh, Ankit Ganeshpurkar, Gopichand Gutti, Ravi Bhushan Singh, Ashok Kumar, and Sushil Kumar Singh. "Combined

structure and ligand-based design of dual BACE-1/GSK-3β inhibitors for Alzheimer's disease." Chemical Papers (2022): 1-18.

7. Ganeshpurkar, Ankit, Rayala Swetha, Devendra Kumar, Gore P. Gangaram, Ravi Singh, Gopichand Gutti, Srabanti Jana, Dileep Kumar, Ashok Kumar, and Sushil K. Singh. "Protein-protein interactions and aggregation inhibitors in Alzheimer's disease." Current topics in medicinal chemistry 19, no. 7 (2019): 501-533.
8. Sharma, Anjali, Rayala Swetha, Nilesh Gajanan Bajad, Ankit Ganeshpurkar, Ravi Singh, Ashok Kumar, and Sushil Kumar Singh. "Cathepsin B-A Neuronal Death Mediator in Alzheimer's Disease Leads to Neurodegeneration." Mini Reviews in Medicinal Chemistry (2022).
9. Ganeshpurkar, Ankit, Ravi Singh, Devendra Kumar, Pravin Gore, Shalini Shivhare, Divya Sardana, Rayala Swetha, Ashok Kumar, and Sushil Kumar Singh. "Identification of sulfonamide based butyrylcholinesterase inhibitors through scaffold hopping approach." International Journal of Biological Macromolecules 203 (2022): 195-211.
10. Bajad, Nilesh Gajanan, Rayala Swetha, Gopichand Gutti, Anjali Sharma, Meenakshi Singh, Ashok Kumar, and Sushil Kumar Singh. "Systematic review on role of structure based drug design (SBDD) in the identification of anti-viral leads against SARS-Cov-2." Current Research in Pharmacology and Drug Discovery 2 (2021): 100026.
11. Bajad, Nilesh Gajanan, Rayala Swetha, Gopichand Gutti, Meenakshi Singh, Ashok Kumar, and Sushil Kumar Singh. "A systematic review of carbohydrate-based bioactive molecules for Alzheimer's disease." Future Medicinal Chemistry 13, no. 19 (2021): 1695-1711.
12. Makar, Subhajit, Tanmay Saha, Rayala Swetha, Gopichand Gutti, Ashok Kumar, and Sushil K. Singh. "Rational approaches of drug design for the development of selective

estrogen receptor modulators (SERMs), implicated in breast cancer." Bioorganic Chemistry 94 (2020): 103380.

13. Saha, Tanmay, Subhajit Makar, Rayala Swetha, Gopichand Gutti, and Sushil K. Singh. "Estrogen signaling: An emanating therapeutic target for breast cancer treatment." European Journal of Medicinal Chemistry 177 (2019): 116-143.

More papers are under preparation and/or review.