Para Substituted Thiosemicarbazones as Cholinesterase Inhibitors: Synthesis, *In vitro* Biological Evaluation and *In silico* Study

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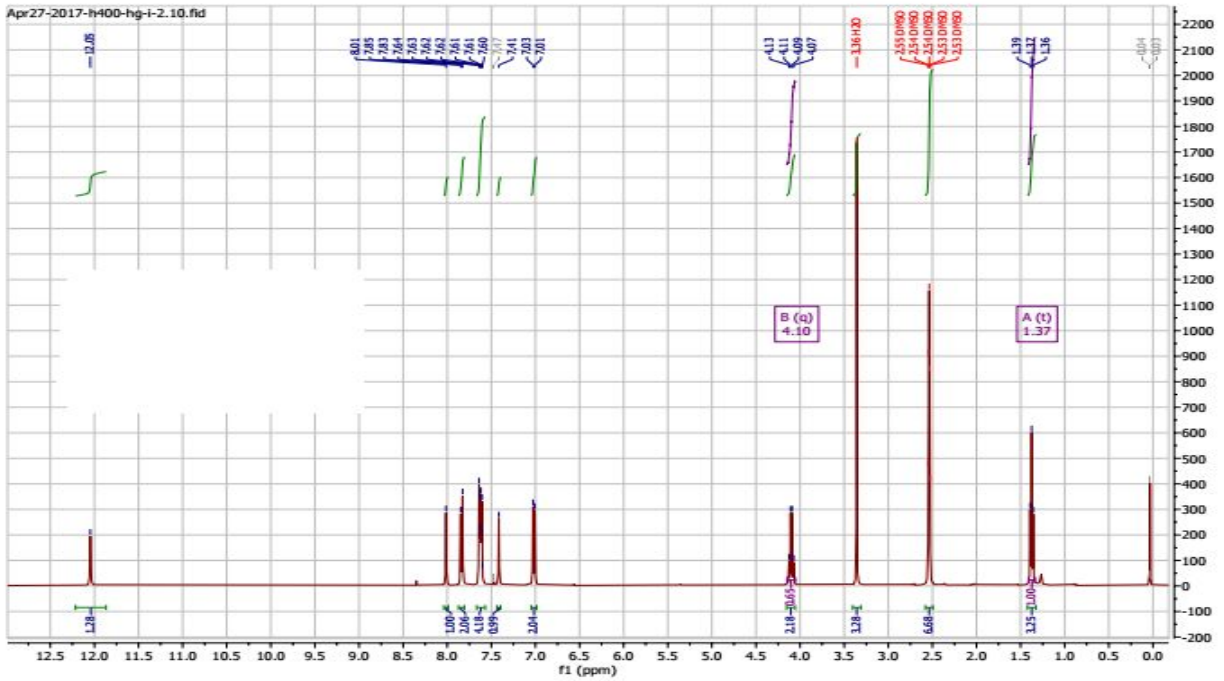


Figure-S1: [1]H-NMR spectra of compound **5**

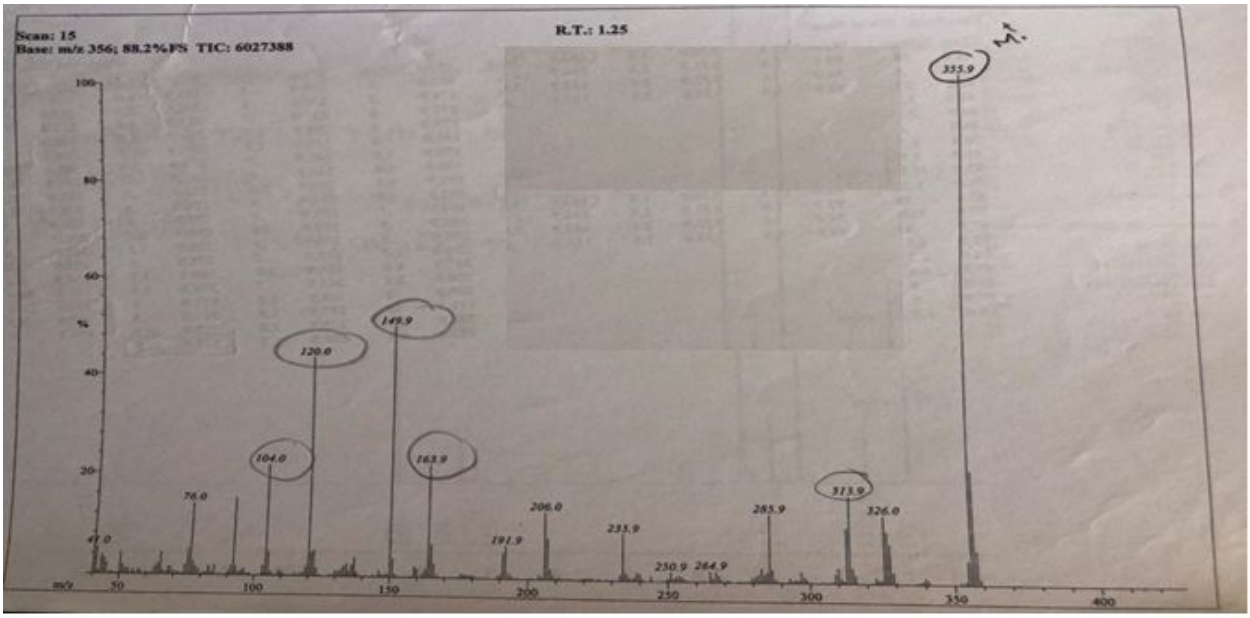


Figure-S2: EI-MS spectra of compound **5**

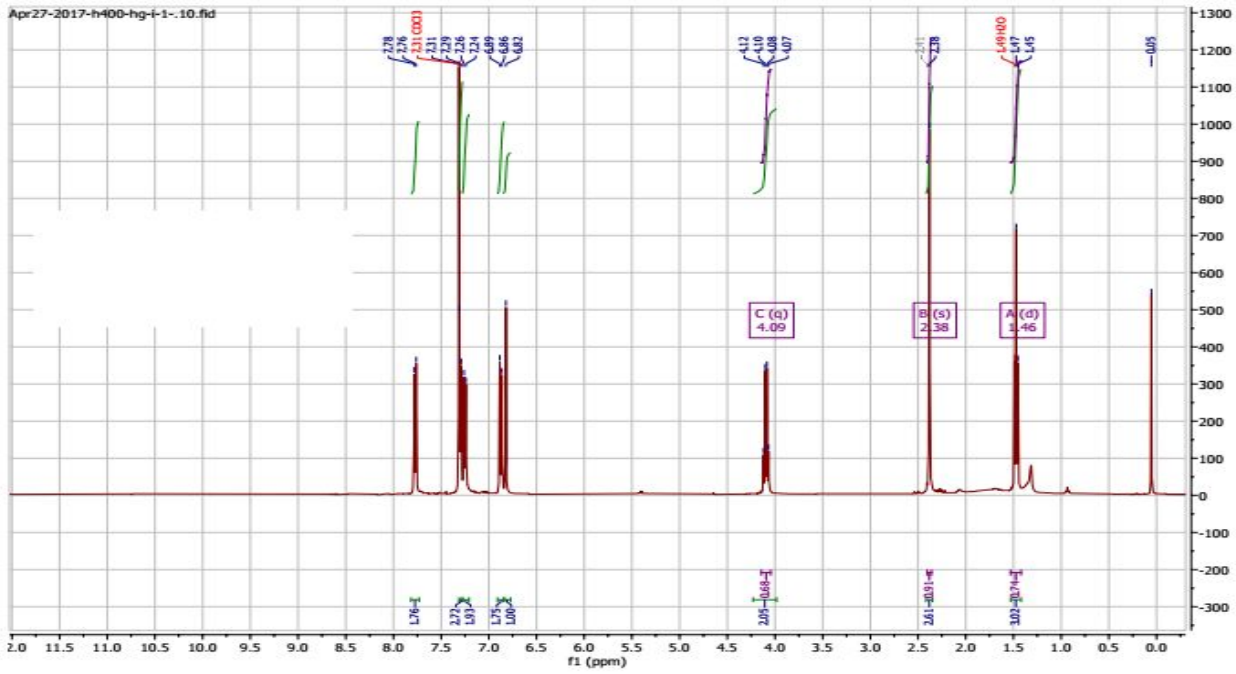


Figure-S3: ^{1}H-NMR spectra of compound **6**

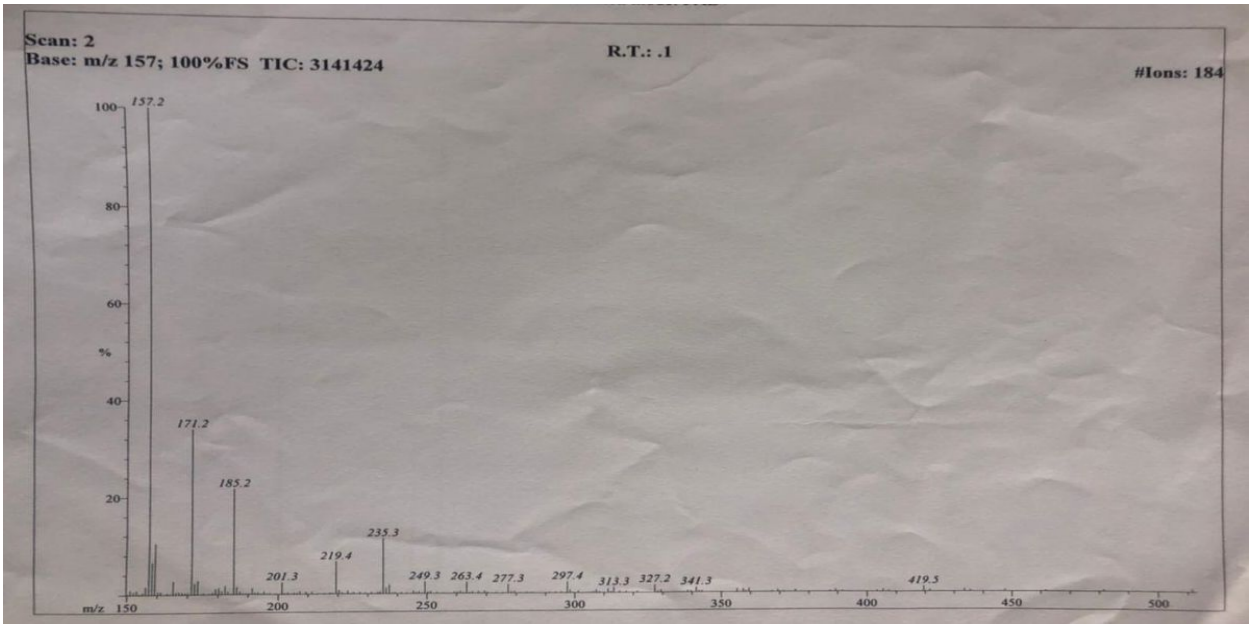


Figure-S4: EI-MS spectra of compound **6**

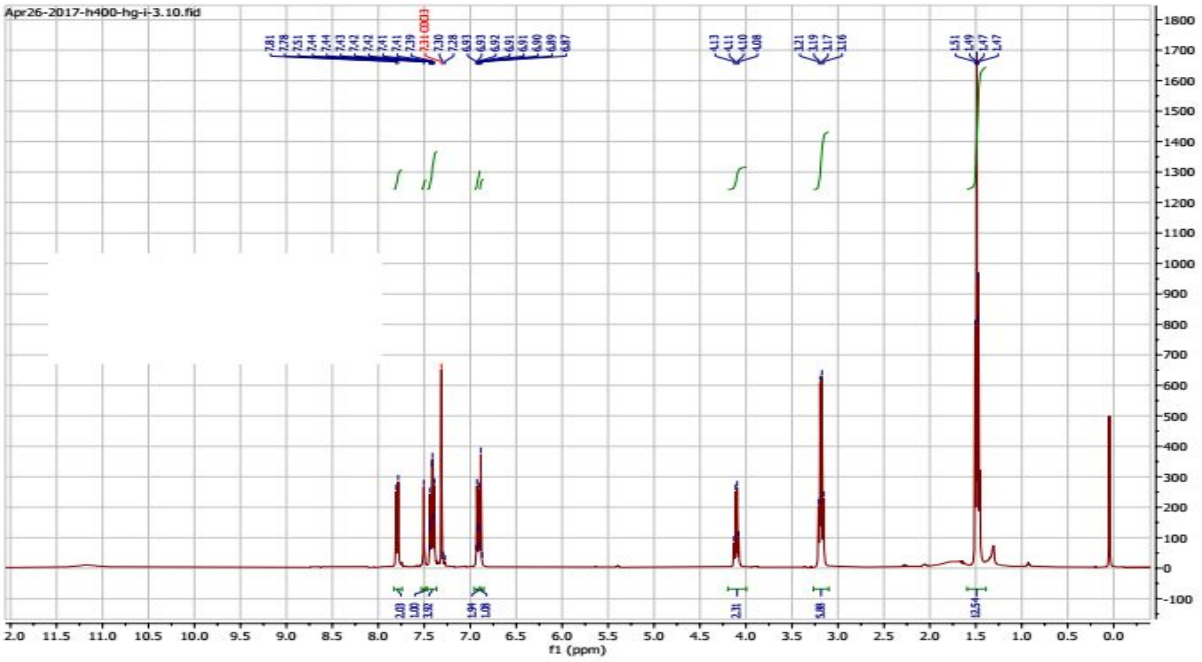


Figure-S5: ^{1}H-NMR spectra of compound **7**

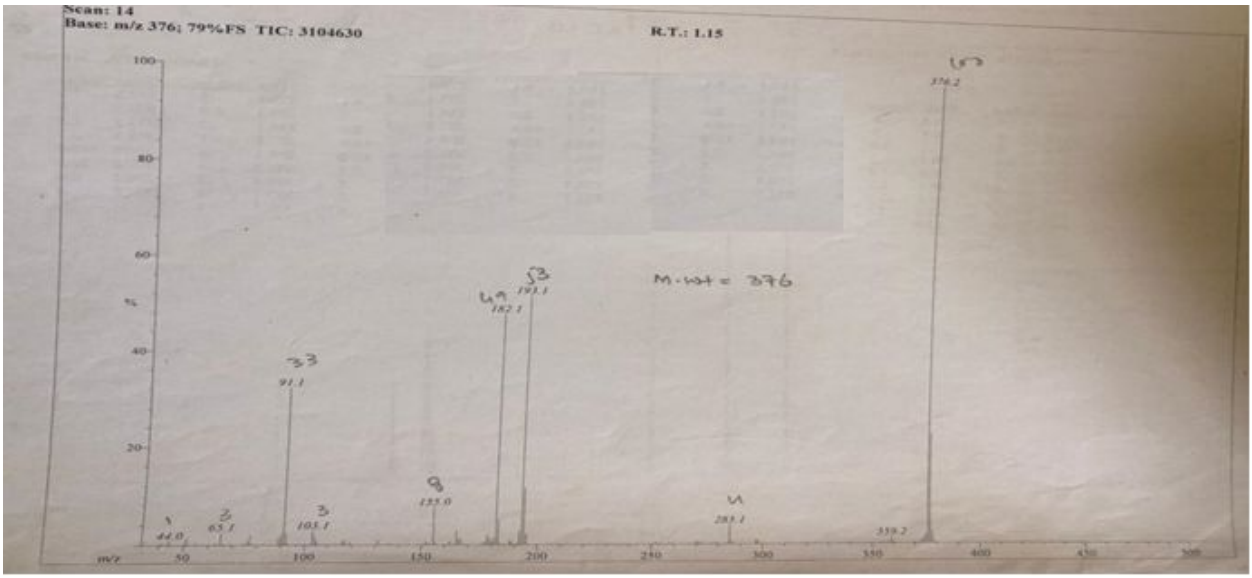


Figure-S6: EI-MS spectra of compound **7**

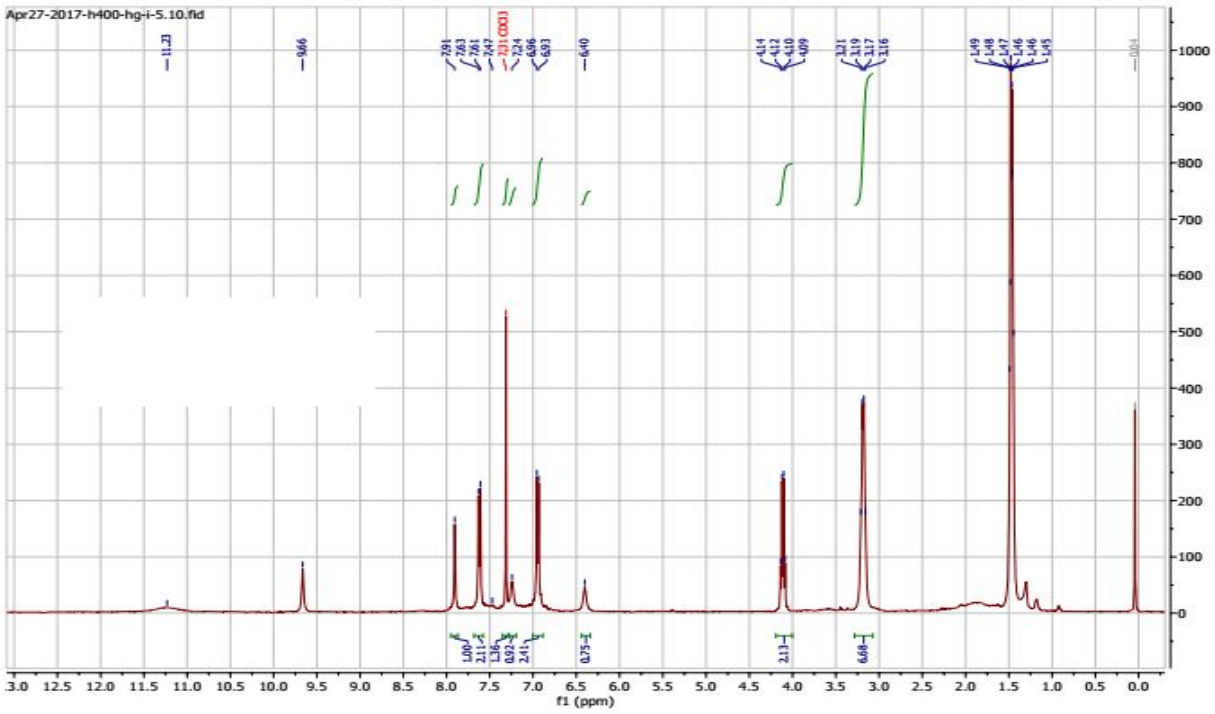


Figure-S7: ^{1}H-NMR spectra of compound **9**

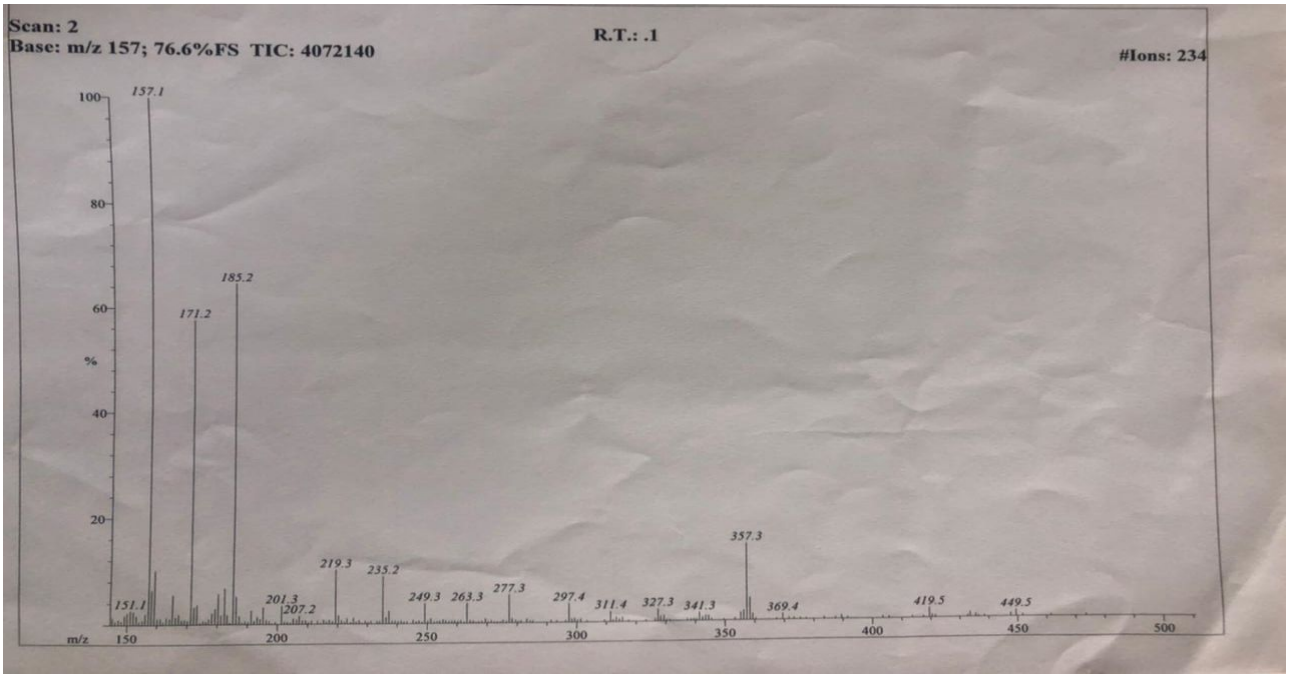


Figure-S8: EI-MS spectra of compound **9**

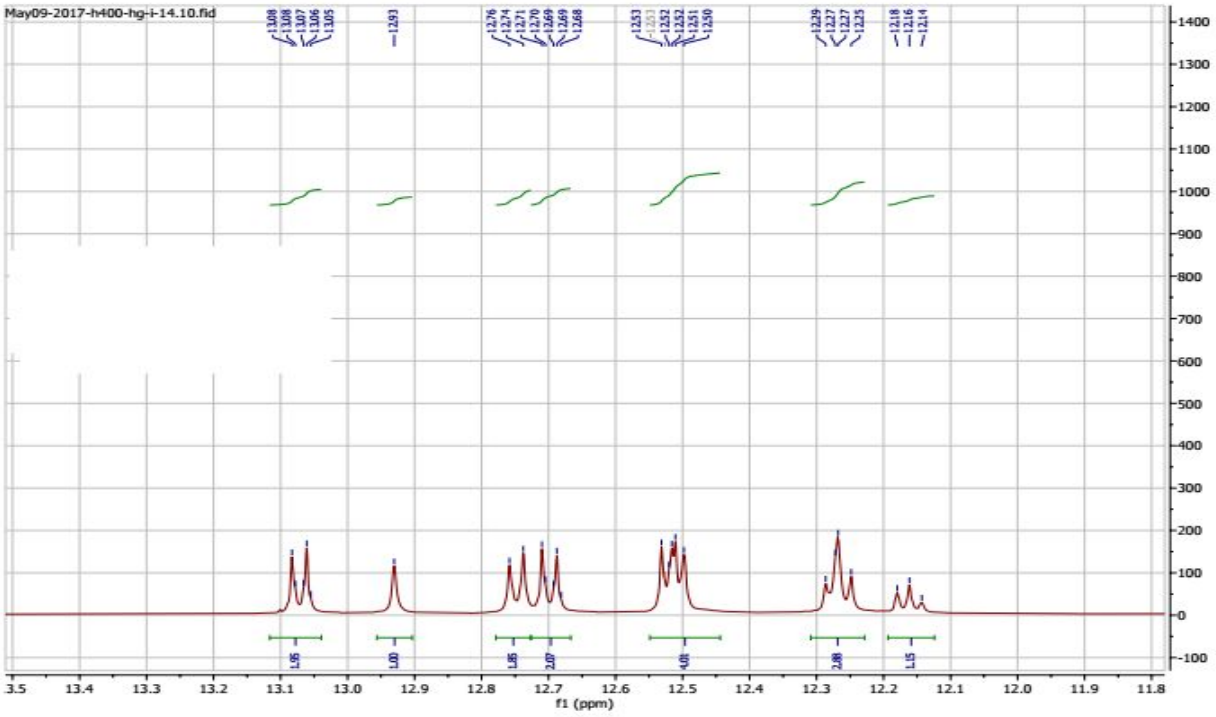


Figure-S9: ^{1}H-NMR spectra of compound **18**

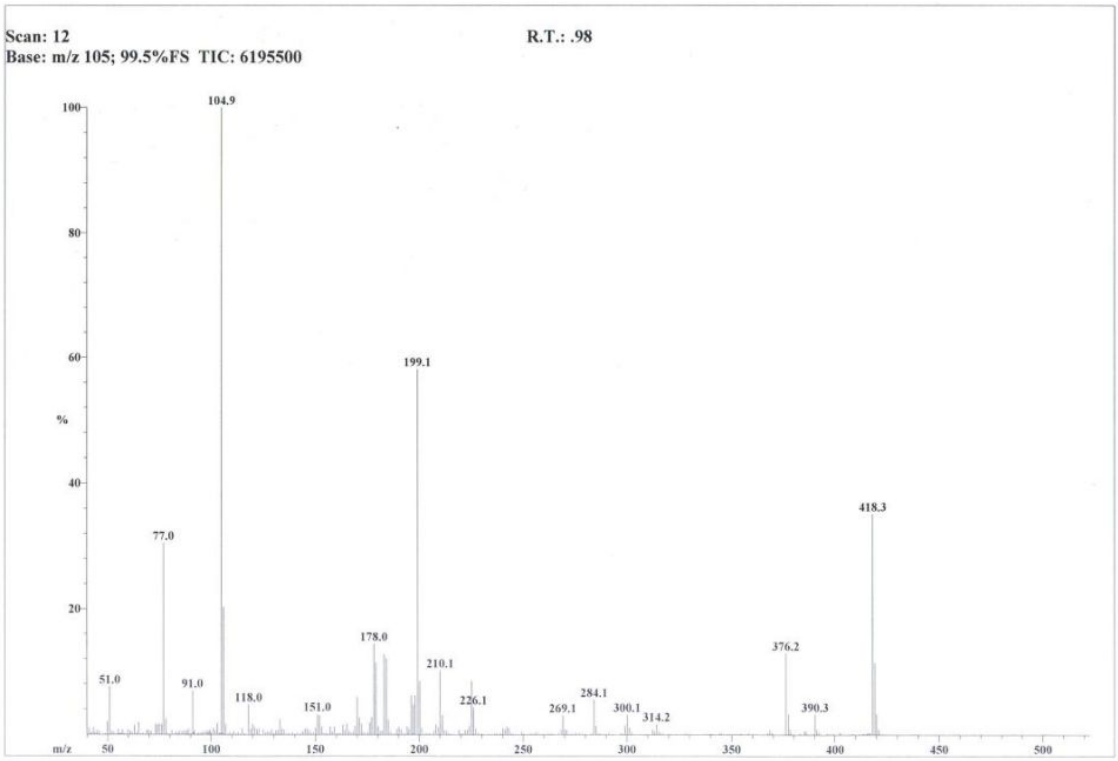


Figure-S10: EI-MS spectra of compound **18**

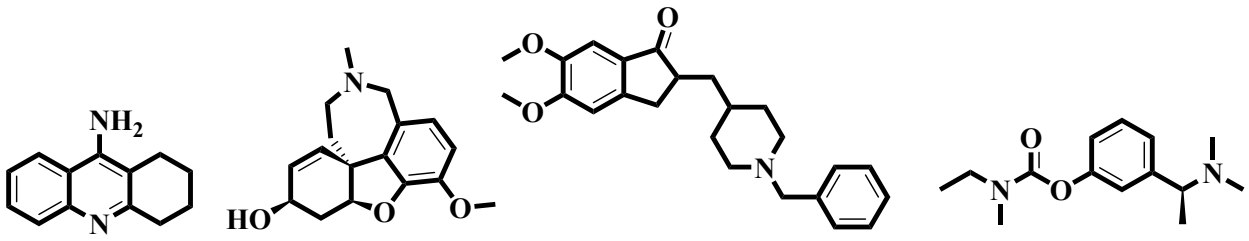


Figure-S11: Marketed available drugs as cholinesterase inhibitors

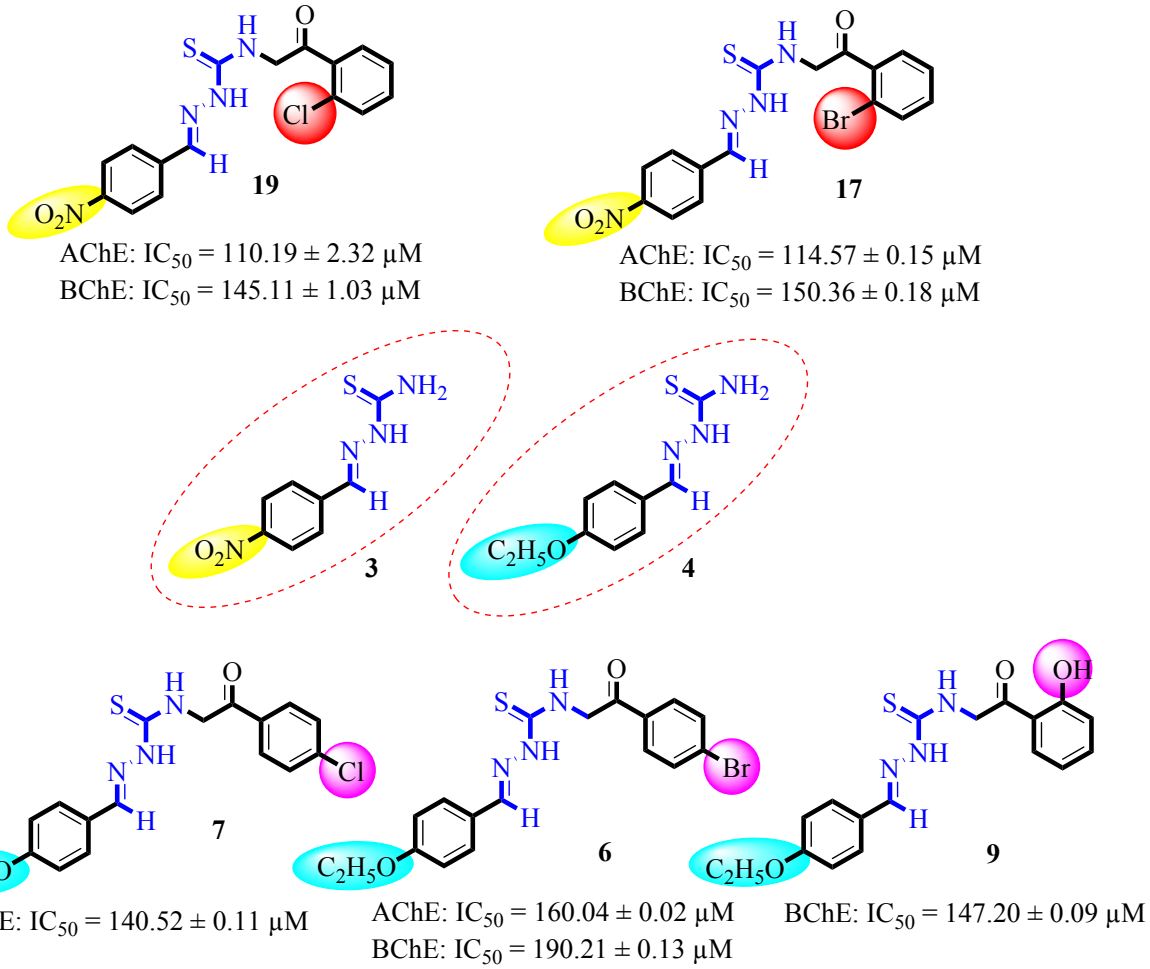


Figure-S12: The most active compounds of the series

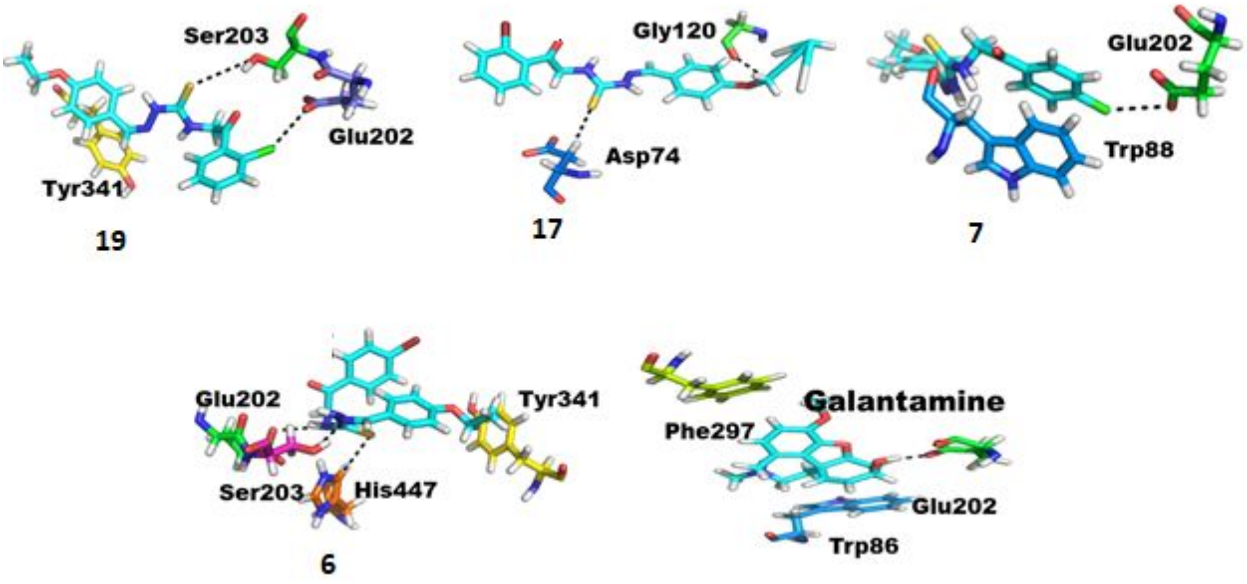


Figure-S13: Protein ligands interaction of acetyl cholinesterase with compounds **19, 17, 7,** and **6** in comparison with galantamine.

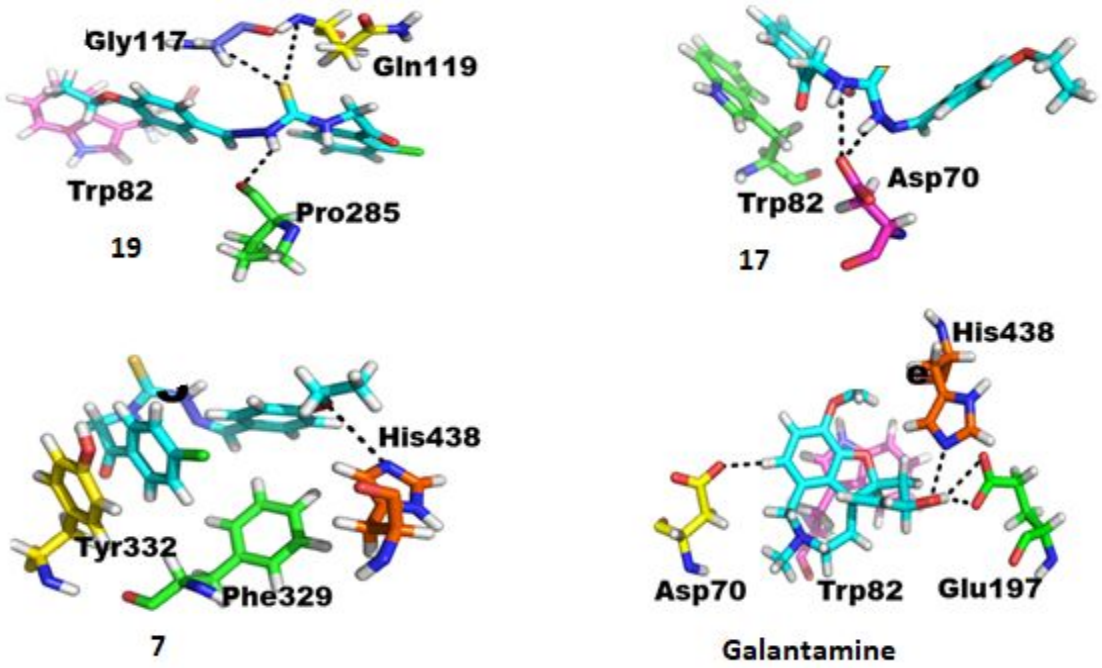
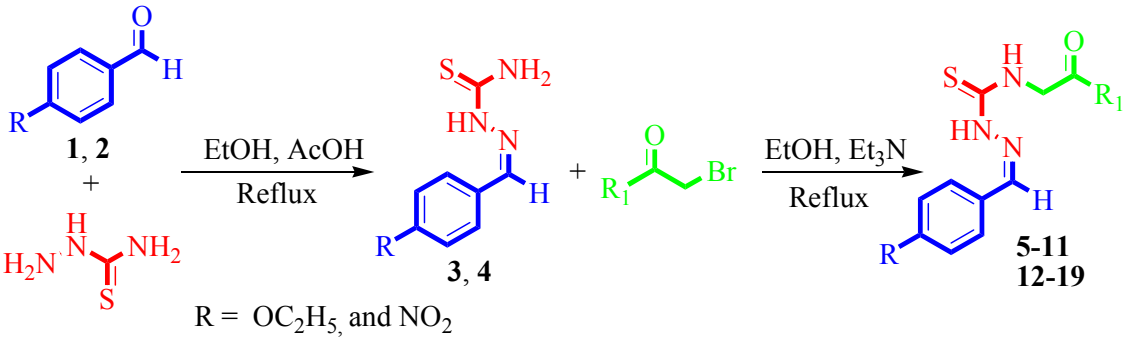
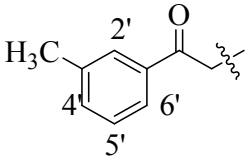
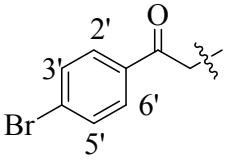
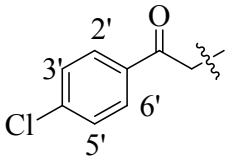
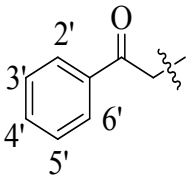
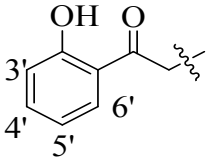
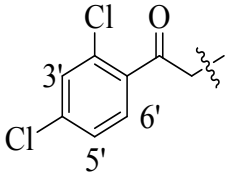
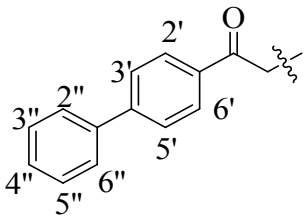
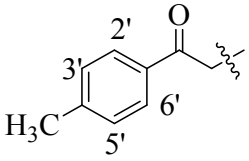


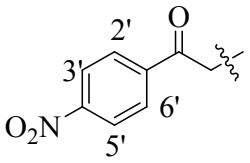
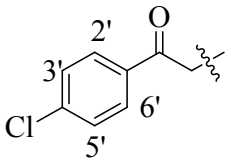
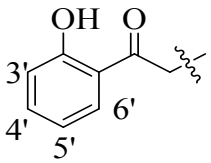
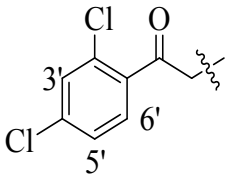
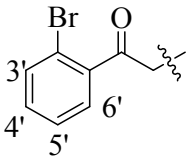
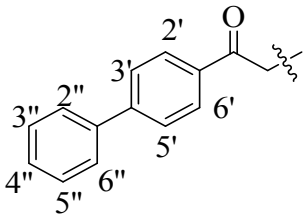
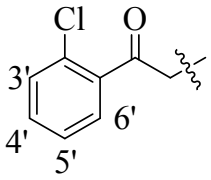
Figure-S14: Protein ligands interaction of butyrylcholinesterase with compounds **19, 17,** and **7** in comparison with galantamine.



Scheme-S1: Thiosemicarbazone derivatives of *para* substituted benzaldehydes **(5-19)**

Table-S1: Acetyl cholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitory activities of compounds **(5-19).**

Compound	R	R_1	AChE	BChE
5	$-OC_2H_5$		295.12 ± 0.12	300.20 ± 0.09
6	$-OC_2H_5$		160.04 ± 0.02	190.21 ± 0.13
7	$-OC_2H_5$		140.52 ± 0.11	334.08 ± 0.05
8	$-OC_2H_5$		220.22 ± 0.14	260.21 ± 0.23
9	$-OC_2H_5$		420.13 ± 0.08	147.20 ± 0.09
10	$-OC_2H_5$		275.71 ± 0.12	330.78 ± 0.10
11	$-OC_2H_5$		460.26 ± 0.14	500.61 ± 0.19
12	$-NO_2$		280.24 ± 0.21	260.38 ± 0.25

13	$-NO_2$		446.37 ± 0.17	326.39 ± 0.23
14	$-NO_2$		340.20 ± 0.26	425.15 ± 0.19
15	$-NO_2$		200.41 ± 0.21	270.26 ± 0.19
16	$-NO_2$		320.36 ± 0.33	306.33 ± 0.28
17	$-NO_2$		114.57 ± 0.15	150.36 ± 0.18
18	$-NO_2$		420.03 ± 0.13	212.25 ± 0.09
19	$-NO_2$		110.19 ± 2.32	145.11 ± 1.03
	Galantamine		104.5 ± 1.20	156.8 ± 1.50

Standard positive control Galanthamine was used, Data is mean ± SEM[a].

Table-S2: Docking scores of compounds **5-19** against Acetyl cholinesterase (AChE).

Compound ID	Docking Score
05	-5.4391
06	-7.5424
07	-5.7615
08	-5.3486
09	-5.1265
10	-5.8769
11	-5.1683
12	-6.3524
13	-56579
14	-6.7932
15	-5.5194
16	-61582
17	-7.3860
18	-5.8361
19	-7.7764
Galantamine	-6.6663

Table-S3: Docking scores of compounds **5-19** against Butyryl cholinesterase (BChE).

Compound ID	Docking Score
05	-5.3645
06	-6.8756
07	-5.6658
08	-5.0978
09	-6.7572
10	-5.6794
11	-5.3355
12	-5.8916
13	-5.3376
14	-6.4673
15	-5.3462
16	-5.9987
17	-7.1376
18	-5.6794
19	-6.8956
Galantamine	-6.5698