Indian Journal of Biochemistry & Biophysics
Vol. 62, July 2025, pp. 786-797
DOI: 10.56042/ijbb.v62i7.16596

Exploring the therapeutic potential of Zonisamide derivatives through molecular docking and dynamic studies with GABARAP

Megha P Nambiar[1], Anakuthil Anoop[2] & Biju AR[3]*

[1]Department of Chemistry, Sir Syed College (Affiliated to Kannur University), Taliparamba, Kannur-670 142, Kerala, India

[2]School of Digital Sciences, Kerala University of Digital Science, Innovation and Technology (Digital University Kerala), Technopark Phase IV, Pallipuram, Thiruvananthapuram-695 317, Kerala, India

[3]Department of Chemistry, Kannur University, Swami Anandatheertha campus, Payyannur-670 327, Kerala, India

Received 22 January 2025; *revised 05 March 2025*

Supplementary Data

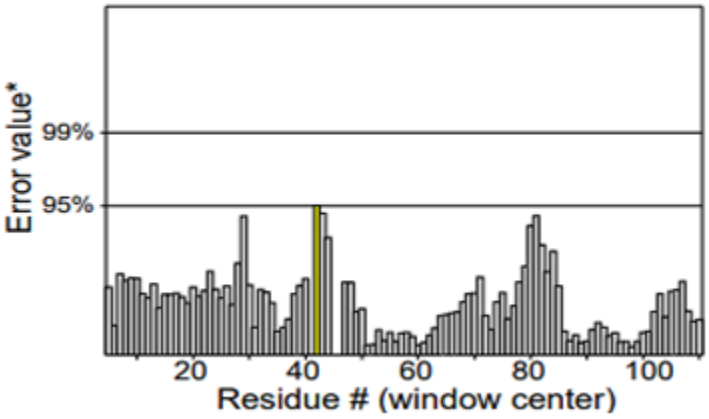

Fig. S1 — Errat plot of modelled GABARAP

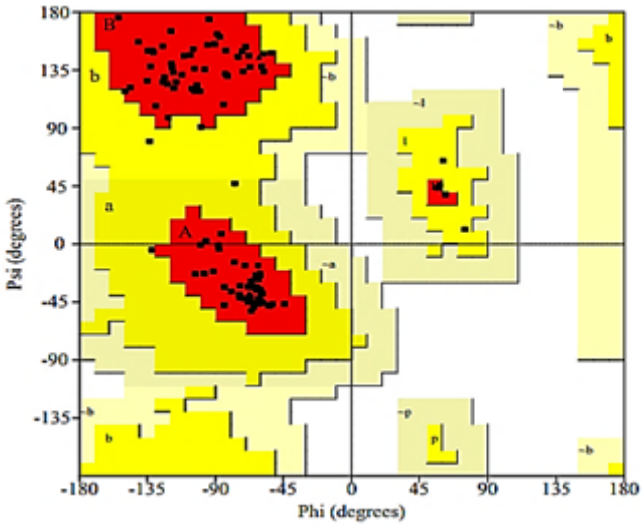

Fig. S2 — Ramachandran plot modelled GABARAP

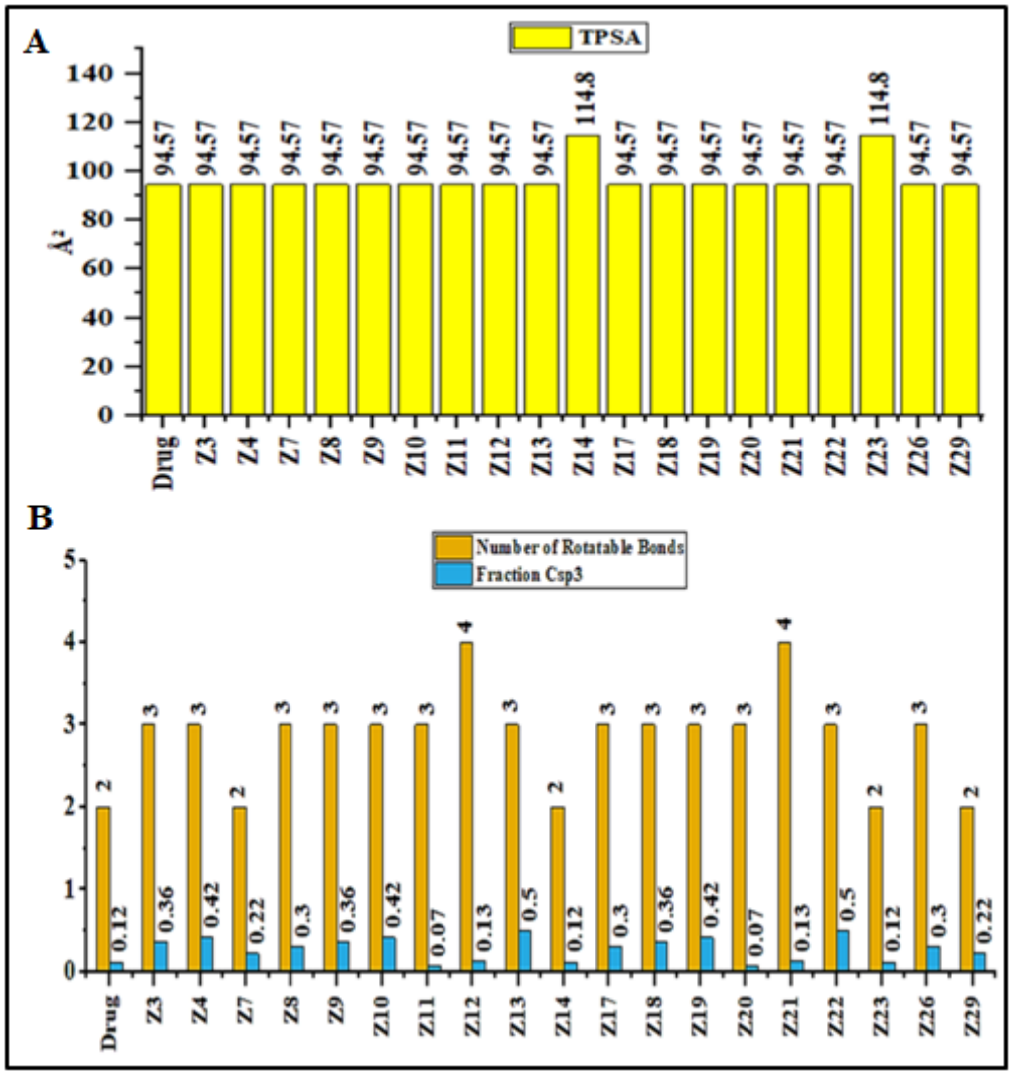

Fig. S3 — Bar graphs showing (A) TPSA; and (B) Number of rotatable bonds, fraction csp^3 of the safe and promising Zonisamide derivatives

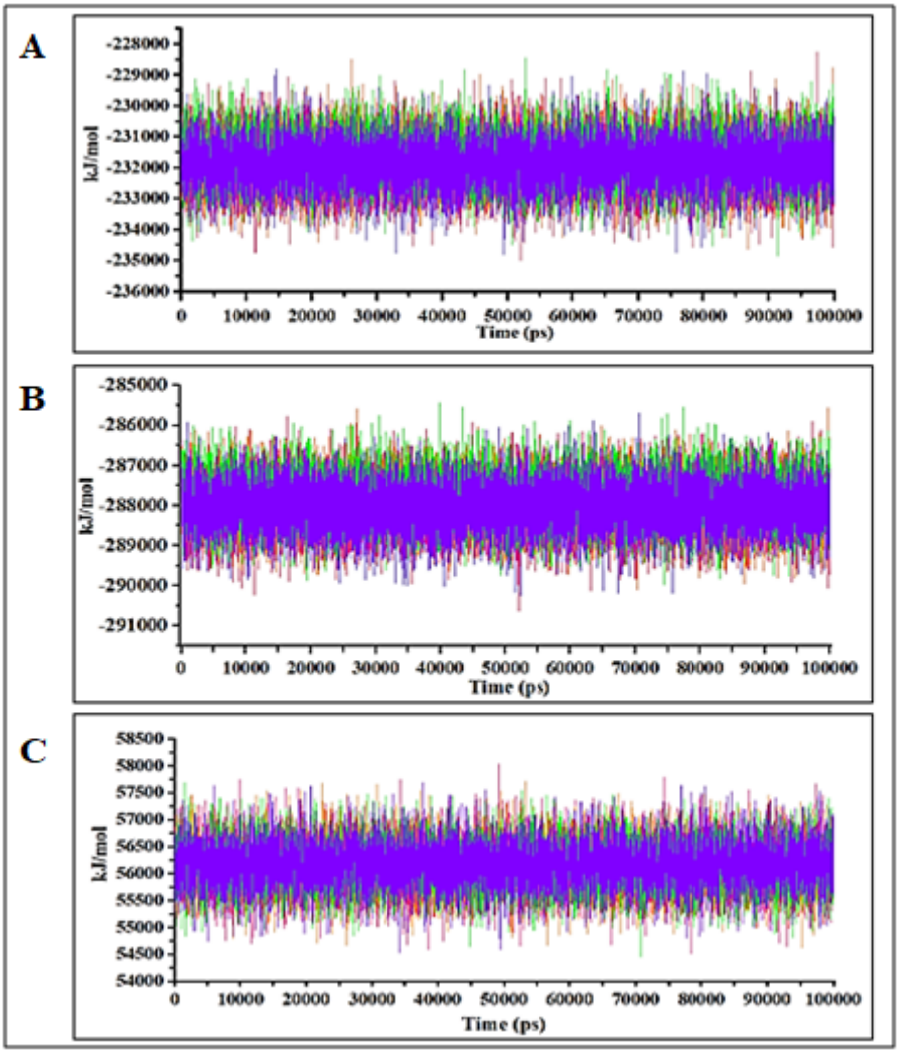

Fig. S4 — (A) Total energy; (B) Potential energy; and (C) Kinetic energy plots of the complexes of Zonisamide-GABARAP (Pink), Z11-GABARAP (Orange), Z20-GABARAP (Green) and Z19-GABARAP (Violet) in the 100 ns

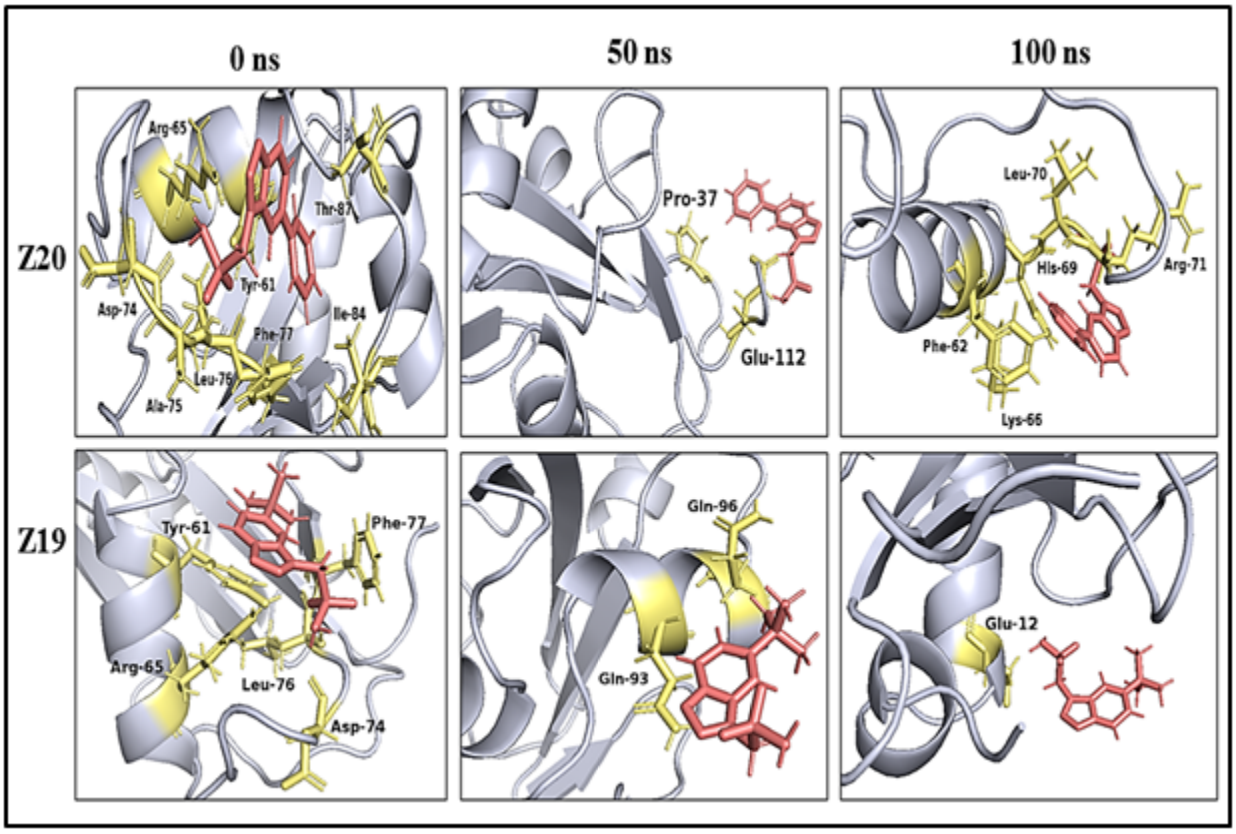

Fig. S5 — Snapshot showing the interacted residues of Z20 and Z19 and Z11 at 0, 50 and 100ns

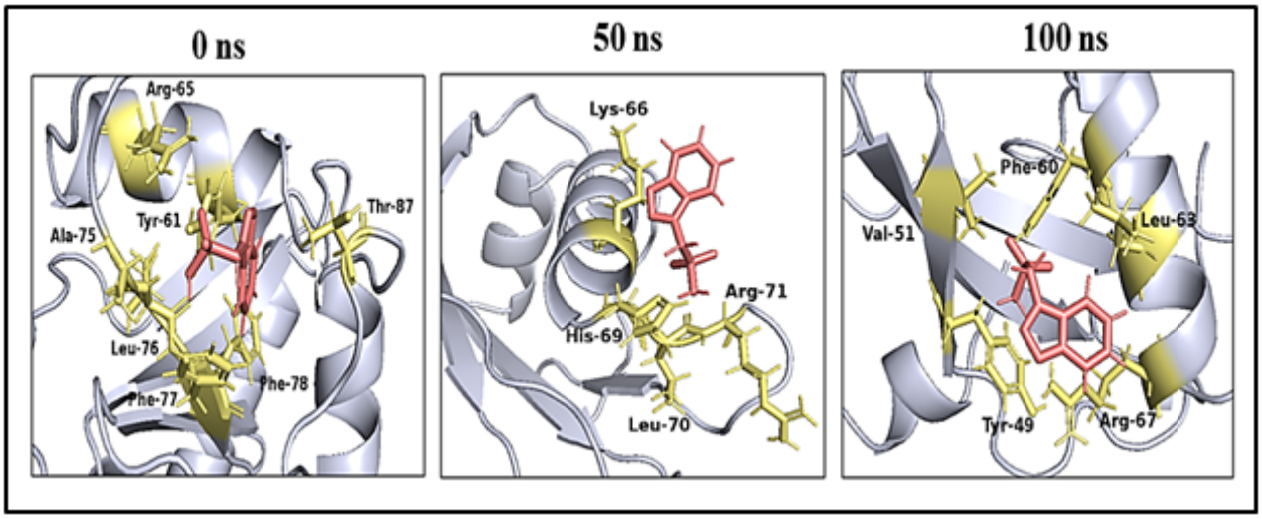

Fig. S6 — Snapshot showing the interacted residues of Zonisamide at 0, 50 and 100ns

Table S1 — IUPAC names of the designed derivatives

Derivatives	IUPAC names
Z1	(7-methylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z2	(7-ethylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z3	(7-isopropylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z4	(7-(tert-butyl)benzo[d]isoxazol-3-yl)methanesulfonamide
Z5	(7-hydroxybenzo[d]isoxazol-3-yl)methanesulfonamide
Z6	(7-aminobenzo[d]isoxazol-3-yl)methanesulfonamide
Z7	(6-methylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z8	(6-ethylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z9	(6-isopropylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z10	(6-(tert-butyl)benzo[d]isoxazol-3-yl)methanesulfonamide
Z11	(6-phenylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z12	(6-benzylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z13	(6-cyclohexylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z14	(6-hydroxybenzo[d]isoxazol-3-yl)methanesulfonamide
Z15	(6-aminobenzo[d]isoxazol-3-yl)methanesulfonamide
Z16	(5-methylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z17	(5-ethylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z18	(5-isopropylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z19	(5-(tert-butyl)benzo[d]isoxazol-3-yl)methanesulfonamide
Z20	(5-phenylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z21	(5-benzylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z22	(5-cyclohexylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z23	(5-hydroxybenzo[d]isoxazol-3-yl)methanesulfonamide
Z24	(5-aminobenzo[d]isoxazol-3-yl)methanesulfonamide
Z25	(4-methylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z26	(4-ethylbenzo[d]isoxazol-3-yl)methanesulfonamide
Z27	(4-hydroxybenzo[d]isoxazol-3-yl)methanesulfonamide
Z28	(4-aminobenzo[d]isoxazol-3-yl)methanesulfonamide
Z29	1-(benzo[d]isoxazol-3-yl)ethanesulfonamide
Z30	1-(benzo[d]isoxazol-3-yl)propane-1-sulfonamide
Z31	benzo[d]isoxazol-3-yl(hydroxy)methanesulfonamide
Z32	amino(benzo[d]isoxazol-3-yl)methanesulfonamide

Table S2 — Rat oral median lethal dose of the derivatives

ID of derivative	Rat LD_{50}
Z3	1600
Z4	1600
Z7	1829
Z8	1257
Z9	1257
Z10	1257
Z11	1257
Z12	1257
Z13	1257
Z14	1829
Z15	1257
Z17	1257
Z18	1257
Z19	1257
Z20	1257
Z21	1257
Z22	1257
Z23	1829
Z24	1257
Z26	1257
Z29	1257

Table S3 — Solubility of promising derivatives based on ESOL model

ID	Log S	Solubility class (ESOL model)
Zonisamide	-1.65	Very soluble
Z3	-2.47	Soluble
Z4	-2.88	Soluble
Z5	-1.5	Very soluble
Z6	-1.28	Very soluble
Z7	-1.94	Very soluble
Z8	-2.2	Soluble
Z9	-2.47	Soluble
Z10	-2.88	Soluble
Z11	-3.16	Soluble
Z12	-3.34	Soluble
Z13	-3.55	Soluble
Z14	-1.5	Very soluble
Z17	-2.2	Soluble
Z18	-2.47	Soluble
Z19	-2.88	Soluble
Z20	-3.16	Soluble
Z21	-3.34	Soluble
Z22	-3.55	Soluble
Z23	-1.5	Very soluble
Z26	-2.2	Soluble
Z29	-1.96	Very soluble