Protein name	PDB accession	Residues used to configure the grid box	Reference
AChE	4EY7	Tyr72, Tyr124 and Ser293	(Alaouy et al., 2023)
AChE	4M0E	Tyr72, Asp74, Tyr124, Trp286, Ser293, Val294, Phe295, Arg296, Phe297, Tyr337, Phe338 and Tyr341	(Faloye et al., 2022)
AChE	4PQE	Ser203, Tyr337, Glu334 and His447	(Marín et al., 2022)
AChE	4EY5	Trp86, Ala204, Phe297, Tyr337, Phe338 and His447	(Işık & Beydemir, 2021)
AChE	4BDT	Thr 83, Trp 86, Gly 121, Gly 122, Ser 203, Tyr 337, Tyr 341 and Trp 439	(Borah et al., 2019)
AChE	1ACJ	Tyr 121, Trp 279, Phe 288, Arg 289 and Tyr 334	(Ali et al., 2017)
AChE	6ZWE	Trp 86, Ser 203, Trp 286, Glu 292, Phe 295, Arg 296, Tyr 337, Tyr 341 and His 447	(Bortolami et al., 2022)
AKT1	2UZS	Lys14 and Arg86.	(Zhen et al., 2023)
Aβ peptide	1Z0Q	His 6, Asp 7, Gly 9, Tyr 10, His 13, His 14, Leu 17, Val 18, Phe 19, Ile 21, Glu 22, Asp 23, Gly 25, Ser 26, Asn 27, Gly 29, Ala 30, Ile 31, Ile 32, Gly 33, Leu 34, Met 35, Val 39, Val 40, Ile 41 and Ala 42	(Castro-Silva et al., 2021)
Aβ peptide	2ONV	Gly2, Val4 and Ala6	(Siddique et al., 2023)
BACE1	2QP8	Leu 91, Asp 93, Tyr 132, Thr 133, Gln 134, Tyr 259, Asp 289, Gly 291, The 293 and Asn 294	(Marín et al., 2022).
BACE1	1FKN	Leu 30, Val 31, Asp 32, Tyr 71, Thr 72, Gln 73, Phe 108, Leu 119 and 228	(Narang et al., 2019)
BACE1	5HU1	Asp 93, Gly 95. Tyr 132, Gln 134, Phe 169, Asp 289 and Gly 291	(Saravanan et al., 2019)

BACE1	5I3V	Gly 11, Leu 30, Val 69, Tyr 71, Trp 76, Phe 108, Ile 110, Trp 115, Ile 118, Thr 232, Asn 233	(Hosen et al., 2018)
BACE1	2FDP	Leu 30, Phe108, Trp 115 and Ile 118	(Dhanabalan et al., 2017)
BACE1	2WJO	Leu 30, Asp 32, Tyr 71, Phe 108, Ile 118, Tyr 198, Ile 226, Asp 228, Gly 230 and Thr 231	(Ali et al., 2017)
BACE1	4DJU	Leu 91, Asp 93, Val 130, Tyr 132, Phe 169 and Asp 289	(da Silva et al., 2023)
BACE1	2OHU	Asp 32, Gly 34, Ser 35, Val 69, Tyr 71, Phe 108, Ile 110, Trp 115 and Thr 231	(El-Nashar et al., 2022)
BuChE	2WID	Asn 57, Asn 256, Thr 258, Lys 469, Glu 482, and Asn 485.	(Borah et al., 2019)
BuChE	1P0P	Trp82 and His438	(Adalat et al., 2023)
BuChE	6ZWI	Trp 82, Ser 198, Trp 231, Pro 285, Phe 329, Tyr 332 and His 438	(Bortolami et al., 2022)
BuChE	4BDS	Trp 82, Gly 116 and Phe239	(Mascarenhas et al., 2021)
BuChE	4TPK	Gly 115, Gly 116, Gly 117, Ser 198, Glu 197, Trp 231, Pro 285, Leu 286, Ser 287, Val 288, Phe 329, Phe 398, His 438.	(Guo et al., 2022)
EGFR	3POZ	Lis 745, Met 766, Leu 788, Thr 790, Met 793, The 854, Leu 858 Leu 788, Arg 803 and Lis 913	(Zu et al., 2021)
GSK-3β	1UV5	Ile 62, Asn 64, Phe 67. Gly 68, Lys 85, Val 135, Pro 136, Arg 141, Lys 183, Gln 185, Asn 186 and Asp 200	(Iwaloye et al., 2020)
MAO-B	4A79	Gly 12, Gly 13, Ile 14, Ser 15, Gly 16, Glu 34, Ala 35, Arg 36, Gly 40, Arg 42, Thr 43, Gly 58, Ser 59, Tyr 60, Gln 65, Val 235, Trp 388, Tyr 398, Thr 426, Gly 434, Met 435 and Glu 437	(Lee et al., 2017)

MAO-B	1GOS	Gly 12, Gly 13, Ile 14, Ser 15, Ala 35, Arg 36, Arg 42, Ser 59, Tyr 60, Leu 171, Val 235, Tyr 326, Trp 388, Tyr 398, Thr 426, Gly 434 and Met 436	(Borah et al., 2019)
MAPK1	1PME	Ala52, Lis54, Thr 105, Met 108, Leu 156 and 167	(Vijh et al., 2023)
MAPK1	5K4I	Ile 31, Val 39, Ala 52, Lis 54, Met 108, Lis 114, Lis 151, Leu 156 and Asp 167	(Zu et al., 2021)
MARK4	5ES1	Ile 62, Val 70, Ala 83, Lys 85, Met 132, ALA 135, Glu 182, Ala 195 and Asp 196	(Naz et al., 2017)
Tau protein	2MZ7	Gln 269, Lys 280, Lys 281, Asp 283, Leu 284, Ser 285, Val 287, Ile 297, Asn 296, Ile 308, Tyr 310 and Pro 312	(Pradeepkiran et al., 2021)

References

Adalat, B., Rahim, F., Rehman, W., Ali, Z., Rasheed, L., Khan, Y., Farghaly, T. A., Shams, S., Taha, M., Wadood, A., Shah, S. A. A., & Abdellatif, M. H. (2023). Biologically Potent Benzimidazole-Based-Substituted Benzaldehyde Derivatives as Potent Inhibitors for Alzheimer's Disease along with Molecular Docking Study. *Pharmaceuticals*, *16*(2), 208. https://doi.org/10.3390/ph16020208

Alaouy, M. A. E., Alaqarbeh, M., Ouabane, M., Zaki, H., ElBouhi, M., Badaoui, H., Moukhliss, Y., Sbai, A., Maghat, H., Lakhlifi, T., & Bouachrine, M. (2023). Computational Prediction of 3,5-Diaryl-1H-Pyrazole and spiropyrazolines derivatives as potential acetylcholinesterase inhibitors for alzheimer disease treatment by 3D-QSAR, molecular docking, molecular dynamics simulation, and ADME-Tox. *Journal of Biomolecular Structure and Dynamics*. https://www.tandfonline.com/doi/full/10.1080/07391102.2023.2252116

Ali, M. Y., Seong, S. H., Reddy, M. R., Seo, S. Y., Choi, J. S., & Jung, H. A. (2017). Kinetics and Molecular Docking Studies of 6-Formyl Umbelliferone Isolated from Angelica decursiva as an Inhibitor of Cholinesterase and BACE1. *Molecules (Basel, Switzerland)*, *22*(10),

1604. https://doi.org/10.3390/molecules22101604

Borah, K., Sharma, S., & Silla, Y. (2019). Structural bioinformatics-based identification of putative plant based lead compounds for Alzheimer Disease Therapy. *Computational Biology and Chemistry*, *78*, 359–366. https://doi.org/10.1016/j.compbiolchem.2018.12.012

Bortolami, M., Pandolfi, F., Tudino, V., Messore, A., Madia, V. N., De Vita, D., Di Santo, R., Costi, R., Romeo, I., Alcaro, S., Colone, M., Stringaro, A., Espargaró, A., Sabatè, R., & Scipione, L. (2022). Design, Synthesis, and In Vitro, In Silico and In Cellulo Evaluation of New Pyrimidine and Pyridine Amide and Carbamate Derivatives as Multi-Functional Cholinesterase Inhibitors. *Pharmaceuticals (Basel, Switzerland)*, *15*(6), 673. https://doi.org/10.3390/ph15060673

Castro-Silva, E. S., Bello, M., Rosales-Hernández, M. C., Correa-Basurto, J., Hernández-Rodríguez, M., Villalobos-Acosta, D., Méndez-Méndez, J. V., Estrada-Pérez, A., Murillo-Álvarez, J., & Muñoz-Ochoa, M. (2021). Fucosterol from Sargassum horridum as an amyloid-beta (Aβ1-42) aggregation inhibitor: In vitro and in silico studies. *Journal of Biomolecular Structure & Dynamics*, *39*(4), 1271–1283. https://doi.org/10.1080/07391102.2020.1729863

da Silva, P. R., de Andrade, J. C., de Sousa, N. F., Ribeiro Portela, A. C., Oliveira Pires, H. F., Bezerra Remígio, M. C. R., Alves, D. da N., de Andrade, H. H. N., Dias, A. L., da Silva Stiebbe Salvadori, M. G., de Oliveira Golzio, A. M. F., de Castro, R. D., Scotti, M. T., Bezerra Felipe, C. F., de Almeida, R. N., & Scotti, L. (2023). Computational Studies Applied to Linalool and Citronellal Derivatives Against Alzheimer's and Parkinson's Disorders: A Review with Experimental Approach. *Current Neuropharmacology*, *21*(4), 842–866. https://doi.org/10.2174/1570159X21666230221123059

Dhanabalan, A. K., Kesherwani, M., Velmurugan, D., & Gunasekaran, K. (2017). Identification of new BACE1 inhibitors using Pharmacophore and Molecular dynamics simulations approach. *Journal of Molecular Graphics & Modelling*, *76*, 56–69. https://doi.org/10.1016/j.jmgm.2017.06.001

El-Nashar, H. A. S., Adel, M., El-Shazly, M., Yahia, I. S., El Sheshtawy, H. S., Almalki, A. A., & Ibrahim, N. (2022). Chemical Composition, Antiaging Activities and Molecular Docking Studies of Essential Oils from Acca sellowiana (Feijoa). *Chemistry & Biodiversity*, *19*(9), e202200272. https://doi.org/10.1002/cbdv.202200272

Faloye, K. O., Mahmud, S., Fakola, E. G., Oyetunde, Y. M., Fajobi, S. J., Ugwo, J. P., Olusola, A. J., Famuyiwa, S. O., Olajubutu, O. G., Oguntade, T. I., & Obaidullah, A. J. (2022). Revealing the Acetylcholinesterase Inhibitory Potential of Phyllanthus amarus and Its Phytoconstituents: In Vitro and in Silico Approach. *Bioinformatics and Biology Insights*, *16*, 11779322221118330. https://doi.org/10.1177/11779322221118330

Guo, Y., Li, S., Zeng, L.-H., & Tan, J. (2022). Tau-targeting therapy in Alzheimer's disease: Critical advances and future opportunities. *Ageing and Neurodegenerative Diseases*, *2*(3), N/A-N/A. https://doi.org/10.20517/and.2022.16

Hosen, S. M. Z., Rubayed, M., Dash, R., Junaid, M., Mitra, S., Alam, M. S., & Dey, R. (2018). Prospecting and Structural Insight into the Binding of Novel Plant-Derived Molecules of Leea indica as Inhibitors of BACE1. *Current Pharmaceutical Design*, *24*(33), 3972–3979. https://doi.org/10.2174/1381612824666181106111020

Işık, M., & Beydemir, Ş. (2021). The impact of some phenolic compounds on serum acetylcholinesterase: Kinetic analysis of an

enzyme/inhibitor interaction and molecular docking study. *Journal of Biomolecular Structure & Dynamics*, *39*(17), 6515–6523. https://doi.org/10.1080/07391102.2020.1801509

Iwaloye, O., Elekofehinti, O. O., Oluwarotimi, E. A., Kikiowo, B. I., & Fadipe, T. M. (2020). Insight into glycogen synthase kinase-3β inhibitory activity of phyto-constituents from Melissa officinalis: In silico studies. *In Silico Pharmacology*, *8*(1), 2. https://doi.org/10.1007/s40203-020-00054-x

Lee, H. W., Ryu, H. W., Kang, M.-G., Park, D., Lee, H., Shin, H. M., Oh, S.-R., & Kim, H. (2017). Potent inhibition of monoamine oxidase A by decursin from Angelica gigas Nakai and by wogonin from Scutellaria baicalensis Georgi. *International Journal of Biological Macromolecules*, *97*, 598–605. https://doi.org/10.1016/j.ijbiomac.2017.01.080

Marín, I. D. G., López, R. H. C., Martínez, O. A., Padilla-Martínez, I. I., Correa-Basurto, J., & Rosales-Hernández, M. C. (2022). New compounds from heterocyclic amines scaffold with multitarget inhibitory activity on Aβ aggregation, AChE, and BACE1 in the Alzheimer disease. *PLOS ONE*, *17*(6), e0269129. https://doi.org/10.1371/journal.pone.0269129

Mascarenhas, A. M. S., de Almeida, R. B. M., de Araujo Neto, M. F., Mendes, G. O., da Cruz, J. N., Dos Santos, C. B. R., Botura, M. B., & Leite, F. H. A. (2021). Pharmacophore-based virtual screening and molecular docking to identify promising dual inhibitors of human acetylcholinesterase and butyrylcholinesterase. *Journal of Biomolecular Structure & Dynamics*, *39*(16), 6021–6030. https://doi.org/10.1080/07391102.2020.1796791

Narang, S. S., Goyal, D., & Goyal, B. (2019). Molecular insights into the inhibitory mechanism of bi-functional bis-tryptoline triazole against β-

secretase (BACE1) enzyme. *Amino Acids*, *51*(10–12), 1593–1607. https://doi.org/10.1007/s00726-019-02797-0

Naz, F., Sami, N., Naqvi, A. T., Islam, A., Ahmad, F., & Imtaiyaz Hassan, M. (2017). Evaluation of human microtubule affinity-regulating kinase 4 inhibitors: Fluorescence binding studies, enzyme, and cell assays. *Journal of Biomolecular Structure & Dynamics*, *35*(14), 3194–3203. https://doi.org/10.1080/07391102.2016.1249958

Pradeepkiran, J. A., Munikumar, M., Reddy, A. P., & Reddy, P. H. (2021). Protective effects of a small molecule inhibitor ligand against hyperphosphorylated tau-induced mitochondrial and synaptic toxicities in Alzheimer disease. *Human Molecular Genetics*, *31*(2), 244–261. https://doi.org/10.1093/hmg/ddab244

Saravanan, K., Sivanandam, M., Hunday, G., Mathiyalagan, L., & Kumaradhas, P. (2019). Investigation of intermolecular interactions and stability of verubecestat in the active site of BACE1: Development of first model from QM/MM-based charge density and MD analysis. *Journal of Biomolecular Structure & Dynamics*, *37*(9), 2339–2354. https://doi.org/10.1080/07391102.2018.1479661

Siddique, Y. H., Naz, F., Rahul, null, Varshney, H., I, M., & Shahid, M. (2023). Effect of donepezil hydrochloride on the transgenic Drosophila expressing human Aβ-42. *The International Journal of Neuroscience*, 1–39. https://doi.org/10.1080/00207454.2023.2262109

Vijh, D., Imam, M. A., Haque, M. M. U., Das, S., Islam, A., & Malik, M. Z. (2023). Network pharmacology and bioinformatics approach reveals the therapeutic mechanism of action of curcumin in Alzheimer disease. *Metabolic Brain Disease*, *38*(4), 1205–1220. https://doi.org/10.1007/s11011-023-01160-3

Zhen, R.-R., Qu, Y.-J., Zhang, L.-M., Gu, C., Ding, M.-R., Chen, L., Peng, X., Hu, B., & An, H.-M. (2023). Exploring the potential anti-

Alzheimer disease mechanisms of Alpiniae Oxyphyliae Fructus by network pharmacology study and molecular docking. *Metabolic Brain Disease*, *38*(3), 933–944. https://doi.org/10.1007/s11011-022-01137-8

Zu, G., Sun, K., Li, L., Zu, X., Han, T., & Huang, H. (2021). Mechanism of quercetin therapeutic targets for Alzheimer disease and type 2 diabetes mellitus. *Scientific Reports*, *11*(1), 22959. https://doi.org/10.1038/s41598-021-02248-5