Journal of the Serbian Chemical Society
JSCS@tmf.bg.ac.rs • www.shd.org.rs/JSCS
*J. Serb. Chem. Soc. 89* (2) S87–S92 (2024) *Supplementary material*

This article has been corrected. See *JSCS* 2024:**89**(3), doi: 10.2298/JSC240325036E

SUPPLEMENTARY MATERIAL TO

# Computer-aided approach for the identification of lead molecules as the inhibitors of cholinesterase's and monoamine oxidases: Novel target for the treatment of Alzheimer's disease

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*J. Serb. Chem. Soc. 89* (2) (2024) 177–194

MOLECULAR DOCKING

*AChE Results:*

**Table S-I**: Binding Energy and bonding and non-bonding interactions of quinolone derivatives within the active pocket of AChE

| Code | Binding Energy (kJ/mol) | Hydrophobic Interactions | H-Bond Interactions | Other Interactions |
|---|---|---|---|---|
| 3 | -21.8 | His447 (π-alkyl) | ------- | Trp86 (π-sigma), Gly120 (Halogen), Tyr123, Tyr337 (π lone pair), Glu202 (unfavorable acceptor-acceptor), Trp286, Asp74, Ser125, Pro88, Leu130, Ala127, Tyr133, Ile451, Gly122, Tyr341, Phe338, Phe297, Val294 (Van der Waals) |
| 3-A | -20.8 | Tyr119 (π-alkyl), Tyr133 (π-alkyl), Leu130 (π-alkyl) | His447 (Conventional H-bond) | Tyr123, Tyr337 (π lone pair), Trp86 (π-sigma), Trp286, Asp74, Ser125, Pro88, Leu130, Ala127, Gly448, Glu202, Tyr341, Phe338, Val294, Phe295 (Van der Waals) |
| 3-B | -20.7 | Tyr119 (alkyl), | His447 | Tyr337 (π lone pair), Trp86 (π- |

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|---|---|---|---|---|
| | | Tyr133 (alkyl), Leu130 (π-alkyl) | (Conventional H-bond) | sigma), Phe295, Val294, Tyr341, Asp74, Gly121, Ser125, Pro88, Gly126, Gly448, Ile451, Glu202, Phe338, (Van der Waals) |
| 3-C | -22.3 | ---------- | Trp86 (Conventional H-bond) Gly126, Gly121 (C-H bond) | Tyr123, Tyr337 (π lone pair), Glu202 (halogen), Arg296, Trp286, Asp74, His447, Gly448, Ser203, Ile451, Leu130, Gly122, Tyr341, Phe338, Phe295 (Van der Waals) |
| 4 | -26.9 | Trp86, Tyr337 (π-π stacked), Pro446 (alkyl), Trp439 (π-alkyl) | His447 (C-H bond) | Ile451, Glu202, Ser203, Tyr133, Gly122, Gly121, Asp74, Tyr341, Thr83, Tyr77 (Van der Waals) |
| 4-A | -26.1 | -------- | Glu202, Gly126 (C-H bond) | Trp86 (π -sigma) Ser203, Tyr133, Gly120, Ala127, Leu130, Pro88, Asp74, His447, Gly448 (Van der Waals) |
| 4-B | -25.6 | Trp86, Tyr337 (π-π stacked), | Thr83 (C-H bond) | Asp74 (π-anion), Trp439, Gly82, Thr83, Asn87, Tyr124, Ser125, Gly121, Gly120, Ser203, Glu202, Ile451, Gly448, Tyr133, Tyr449 (Van der Waals) |
| 4-C | -26.5 | Trp86, Tyr337 (π-π stacked), Trp86 (π-alkyl) | ---------- | Thr83, Asp74, Tyr124, Gly121, Gly126, Gly120, Tyr133, Glu202 Ile451, Gly448, Pro446, Tyr449, Trp439, Gly82 (Van der Waals) |
| Huprine | -29.5 | Trp86, Tyr337 (π-π stacked), His447 (alkyl), Trp439, Pro446, Tyr449 (π-alkyl) | Ser203 (C-H Bond) | Phe295, Phe297, Ala204, Gly122, Phe338, Gly121, Ser125, Tyr341, Ile451 (Van der Waals) |

*BChE Results:*

**Table S-II**: Binding Energy and bonding and non-bonding interactions of quinolone derivatives within the active pocket of BChE

| Code | Binding Energy (kJ/mol) | Hydrophobic Interactions | Hydrogen Bond Interactions | Other Interactions |
|---|---|---|---|---|
| 3 | -28.6 | Gly116 (π- π T shaped), Trp82 (Amide π stacked), Ala328 (π-alkyl), Ser287 (Halogen) | ------- | Tyr440, Gly439, Thr120, Gln119, Trp231, Val288, Gly117, Ser198, Phe328, Phe398, Ser79, Gly78, Trp430, Met437 (Van der Waals) |
| 3-A | -26.5 | Gly116 (Amide π stacked), His438 (π-alkyl) | Gly117, Ser198 (conventional H-bond) | Phe398, Ala199, Trp231, Phe329, Pro285, Ser287, Asn289, Gln119, Thr120 (Van der Waals) |
| 3-B | -26.6 | Gly116 (Amide π stacked), Val288 (π-alkyl), Ala277 (alkyl) | Ser198, Gly117 (conventional H-bond) | Asn289, Gln119, Thr120, Phe398, Ala199, Trp231, Leu286, Phe329 Van der Waals) |
| 3-C | -29.3 | Phe329, Trp231 (π- π T shaped), His438, Leu286 (π-alkyl) | Thr122, Tyr128 (conventional H-bond), Gly121 (C-H bond) | Trp82 (π-sigma), Glu197 (unfavorable acceptor-acceptor) Val288, Pro285, Gly116, Leu125, Gly115, Ile442, Gly439, Phe398 (Van der Waals) |
| 4 | -24.1 | Tyr128 (π-alkyl) | -------- | Trp82 (π-sigma), Tyr440, Ser198, Gl197, Gly116, Gly115, Thr122, Asn83, Thr120, Asp70 (Van der Waals) |
| 4-A | -25.3 | His438 (π-alkyl) | Tyr128(Conventional H-bond) | Ser198, Gly115, Thr122, Tyr114, Leu125, Pro84, Asn83, Thr120, Asp70, Gly439 (Van der Waals) |
| 4-B | -25.2 | Trp82 (alkyl), | Trp82, Tyr128 | Ser198, Gly115, |

| | | | | |
|---|---|---|---|---|
| | | His438 (π-alkyl) | (Conventional H-bond), Gly121 (C-H bond) | Leu125, Thr122, Asn83, Asp70, Gly116, Gly439 (Van der Waals) |
| 4-C | -24.9 | His438 (π-alkyl) | Gly121 (C-H bond) | Glu197, Ser198, Gly116, Gly115, Pro84, Asn83, Thr120, Asp70, Gly439 (Van der Waals) |
| Donepezil | -30.6 | Gly121 (π-π stacked), Tyr337, Trp439 (Amide-π stacked) | Tyr83, His447, Glu202, Thr83 (C-H Bond) | Ile451, Asn87, Asp74, Tyr449, Ser125, Tyr124, Gly122(Van der Waals) |

*MAO-A Results:*

**Table S-III:** Binding Energy and bonding and non-bonding interactions of quinolone derivatives within the active pocket of MAO-A

| Code | Binding Energy (kJ/mol) | Hydrophobic Interactions | Hydrogen Bond Interactions | Other Interactions |
|---|---|---|---|---|
| 3 | -37.5 | Trp397 (π- π stacked), Tyr444 (Amide-π stacked), Tyr407 (π-π stacked), Met445, Ala448 (π-alkyl), | Thr52 (Conventional H-bond) Ile23 (π-donor hydrogen bond) | Ser24, Gly434, Thr435, Gly66, Lys305, Phe352, Ala68, Gly50 (Van der Waals) |
| 3-A | -37.5 | Tyr407 (π- π stacked), Tyr407 (Amide-π stacked), Tyr407 (π-π stacked), Phe352, Cys406 (alkyl), Ala448 (π-alkyl Gly49 (halogen) | Arg51, Thr52 (Conventional H-bond) Tyr444 (H-bond donor) | Met445 (π-sulphur), Ala272, Ser24, Gly434, Thr435, Gln215, Val303, Lys305, Gly66, Gly67, Ile23 (Van der Waals) |
| 3-B | -37.1 | Gln215 (Halogen) Ala448 (alkyl), Cys406, Met445 (π-alkyl) | Tyr444 (C-H bond) | Arg51 (π-cation), Ala272, Ile273, Ser24, Gly434, Thr435, Ala68, Gly214, Gln74, Phe352, Lys305, Gly67 (Van der Waals) |
| 3-C | -36.9 | Trp397 (Amide-π stacked), Tyr407 (π-π stacked), Val303 (alkyl), Met445, Ala448 (π- | ------ | Arg51 (π-cation), Gly434, Ser24, Ala272, Gly49, Ile23, Thr52, Gly66, Lys305, Phe352, Ala68, |

| | | | | |
|---|---|---|---|---|
| | | alkyl) | | Gly443 (Van der Waals) |
| 4 | -30.3 | Gly66 (Amide- π stacked), Arg51 (alkyl), Phe352 (π-alkyl) | Tyr407, Gly443 (C-H bond) | Gly67, Lys305, Gln215, Gly214, Tyr444, Ala448, Thr435, Ile23, Thr52 (Van der Waals) |
| 4-A | -29.1 | Gly66 (Amide- π stacked), Met445 (π-alkyl) | Tyr407 (C-H bond) | Cys406 (π-Sulphur), Ala448, Arg51, Ile23, Thr52, Gly67, Lys305, Phe352, Gln215, Gly214, Gln74, Thr435, (Van der Waals) |
| 4-B | -28.4 | Trp397 (Amide- π stacked), Gly66 (π-π T shaped), Arg51 (alkyl), Met445 (π-alkyl) | Gly67 (C-H bond) | Ala448, Thr435, Ile23, Thr52, Tyr444, Phe352, Tyr444, Thr52, Ile23, Thr435 (Van der Waals) |
| 4-C | -29.5 | Trp397 (Amide- π stacked), Gly66 (π-π T shaped), Arg51 (alkyl) | Tyr407, Gly443 (C-H bond) | Ile23, Lys305, Phe352, Gln215, Thr435, Aal448, Thr52, Ile23 (Van der Waals) |
| Clorgyline | -29.8 | Lys102 (alkyl), Lys357 (π-alkyl) | Glu329, Asp328, Asn179 (C-H bond) | Arg172 (π-cation), Val101, Tyr175, Ile326, Glu185, Leu354, Ala355, Ser334 (Van der Waals) |

*MAO-B Results:*

**Table S-IV:** Binding Energy and bonding and non-bonding interactions of quinolone derivatives within the active pocket of MAO-B

| Code | Binding Energy (kJ/mol) | Hydrophobic Interactions | Hydrogen Bond Interactions | Other Interactions |
|---|---|---|---|---|
| 3 | -34.9 | Tyr398 (π- π stacked), Trp338 (π- π T shaped), Gly57 (Amide-π stacked), Gly40 (Halogen), Ala439 (π-alkyl) | ------- | Arg42 (π-cation) Ser15, Thr426, Gly58, Val294, Lys296, Phe343, Tyr60, Tyr435, Thr43, Gly13, Ala263, Gly425 (Van der Waals) |
| 3-A | -36.7 | Tyr398 (π- π stacked), Ala439 (alkyl), Cys397, Phe343 (π- | Gly58 (C-H bond), Arg42 (Conventional H-Bond) | Thr43 (π-cation), Gly13, Ala263, Ser15, Gly425, Thr426, Gly434, Thr435, Gly57, Val294 |

| | | | | |
|---|---|---|---|---|
| | | alkyl) | | (Van der Waals) |
| 3-B | -36.9 | Trp388 (π- π stacked), Tyr398 (π- π T shaped), Ala439 (alkyl), Lys296, Val294, Cys397, Phe343 (π-alkyl) | ------ | Arg42 (π-cation), Ala263, Ile264, Gly13, Ile14, Thr43, Gly57, Leu56, Tyr435, Gly434, Thr426, Gly425, Ser15 (Van der Waals) |
| 3-C | -35.9 | Trp388 (π- π stacked), Tyr398 (π- π T shaped), Ala439 (alkyl) | ------ | Arg42 (π-cation), Ala263, Ile264, Gly13, Ile14, Gly40, Gly57, Leu56, Val294, Lys296, Phe343, Ser59, Tyr435, Gly434, Gly425(Van der Waals) |
| 4 | -28.6 | Val294, Tyr398 (alkyl), Met436 (π-alkyl) | --------- | Cys397 (π-Sulphur) Gly57,Gly434, Ser59, Tyr60, Lys296, Leu56, Trp388 (Van der Waals) |
| 4-A | -27.7 | Tyr435 (π-π stacked), Cys397 (π-alkyl) | Lys296 (Conventional H-bond) Tyr398, Arg42 (C-H Bond) | Thr43, Ile14, Gly58, Phe343, Gly434, Thr426 (Van der Waals) |
| 4-B | -28.5 | Gly57 (Amide- π stacked), Trp388 (π-π T shaped), Lys296 (alkyl), Cys397 (π-alkyl) | Tyr398 (C-H bond) | Ile14, Tyr435, Gly58, Tyr60, Phe343, Val294, Arg42, Thr426, Ala439, Gly434, Thr43 (Van der Waals) |
| 4-C | -28.7 | Val294 (alkyl), Arg42 (π-alkyl) | Tyr435 (C-H bond) | Cys397 (π-sulphur), Thr426, Gly434, Gly58, Phe343, Lys296, Leu56, Trp388 (Van der Waals) |
| Deprenyl | -22.5 | Phe103,Val106, Trp119, His115, Leu164 (alkyl), Tyr112 (π-alkyl) | --------- | Glu483 (π-anion), Asn116, Thr196, Thr478, Thr479, Arg120 (Van der Waals) |