An in silico analysis of Ibuprofen enantiomers in high concentrations of sodium chloride with SARS-CoV-2 main protease

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Resumen

2020 will be remembered worldwide for the outbreak of Coronavirus disease (COVID-19), which quickly spread until it was declared as a global pandemic. The main protease (Mpro) of SARS-CoV-2, a key enzyme in coronavirus, represents an attractive pharmacological target for inhibition of SARS-CoV-2 replication. Here, we evaluated whether the anti-inflammatory drug Ibuprofen, may act as a potential SARS-CoV-2 Mpro inhibitor, using an in silico study. From molecular dynamics (MD) simulations, we also evaluated the influence of ionic strength on the affinity and stability of the Ibuprofen–Mpro complexes. The docking analysis shows that R(−)Ibuprofen and S(+)Ibuprofen isomers can interact with multiple key residues of the main protease, through hydrophobic interactions and hydrogen bonds, with favourable binding energies (−6.2 and −5.7 kcal/mol, respectively). MM-GBSA and MM-PBSA calculations confirm the affinity of these complexes, in terms of binding energies. It also demonstrates that

the ionic strength modifies significantly their binding affinities. Different structural parameters calculated from the MD simulations (120 ns) reveal that these complexes are conformational stable in the different conditions analysed. In this context, the results suggest that the condition 2 (0.25 NaCl) bind more tightly the Ibuprofen to Mpro than the others conditions. From the frustration analysis, we could characterize two important regions (Cys44-Pro52 and Linker loop) of this protein involved in the interaction with Ibuprofen. In conclusion, our findings allow us to propose that racemic mixtures of the Ibuprofen enantiomers might be a potential treatment option against SARS-CoV-2 Mpro. However, further research is necessary to determinate their possible medicinal use. Communicated by Ramaswamy H. Sarma.

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