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A computational effort to untangling anti-SARS-CoV-2 effects of oleanolic acid analogues

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Abstract: Considering the current global pandemic and the urgent need to introduce novel drug candidates against severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), we reported at least four antipyretic recipes of Kurdish ethno medicine which can be translated to functional antiviral formulations in orthodox medicine (Mohammed, 2020). Our current demanding computational work places much emphasis upon the implications of oleanolic acid and its analogues as a cluster of binder candidates of the main protease (M^{pro}) of SARS-CoV-2 which having a pivotal role in the pathogenesis of coronavirus disease 2019 (COVID-19). Through molecular docking and simulation studies, we found oleanolic acid (-12.6 Kcal/mol) and its two analogues (OA11; ligand I (-14.2 Kcal/mol)) and (OA31; ligand II (-14.0 Kcal/mol)) bound with M^{pro} (PDB: 6Y84) more reliable and trustful than saquinavir (-8.1 Kcal/mol) as a canonical drug. Salaspermic acid, (3b)-3-{[(2E)-3-phenylprop-2-enoyl]oxy}olean-12-en-28-oic acid, OA37 and OA40 interacted with catalytic dyad and major amino acid residues of active sites of M^{pro} and these toxic compounds should be considered in future anti-protease drug design. Overall, the current study seized the attention of experimentalists to the new set of anti-protease pentacyclic triterpenoids that should to be assayed against SARS-CoV-2 at *in vitro* or in clinical settings of COVID-19.

Keywords: Main Protease; M^{pro}; COVID-19; oleanolic; acid toxicity; computational biology