

Supporting Information

Procainamide-SAHA fused inhibitors of hHDAC6 tackle multi-drug resistant malaria parasites

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Additional molecular modelling data

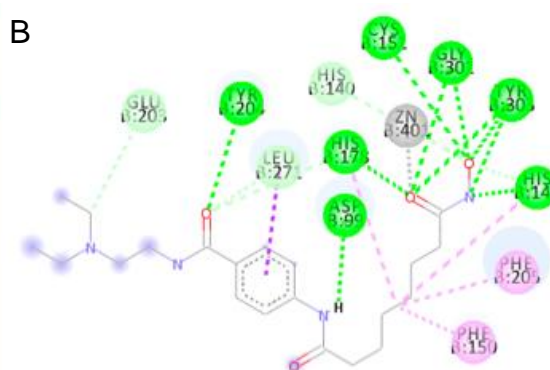
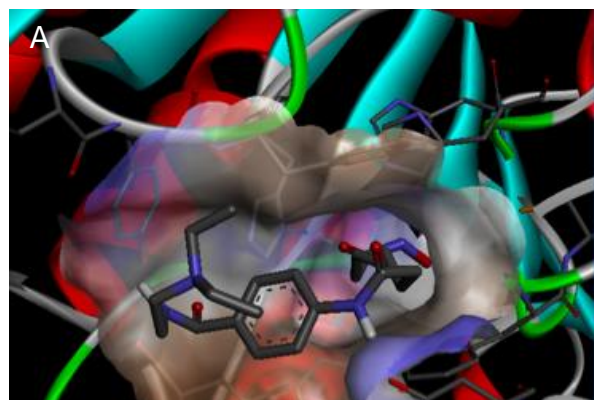
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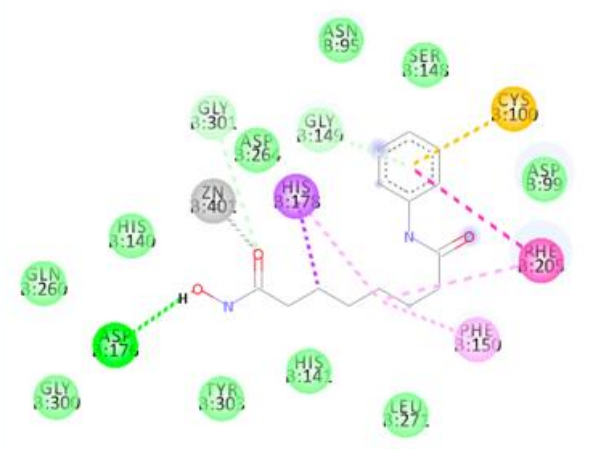
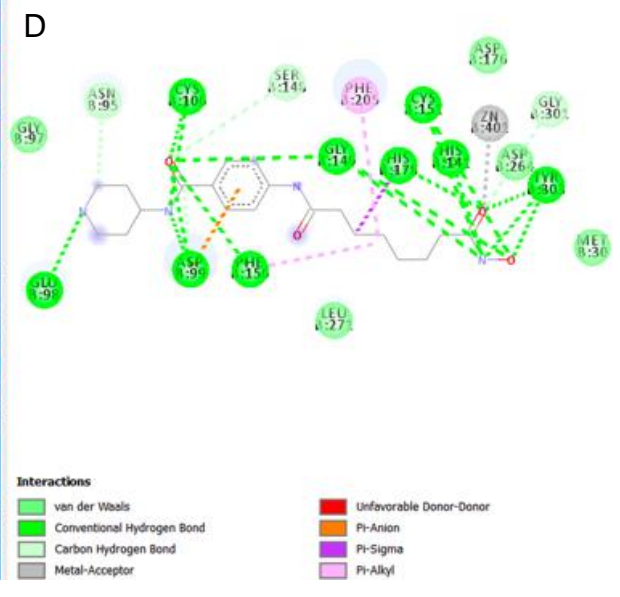
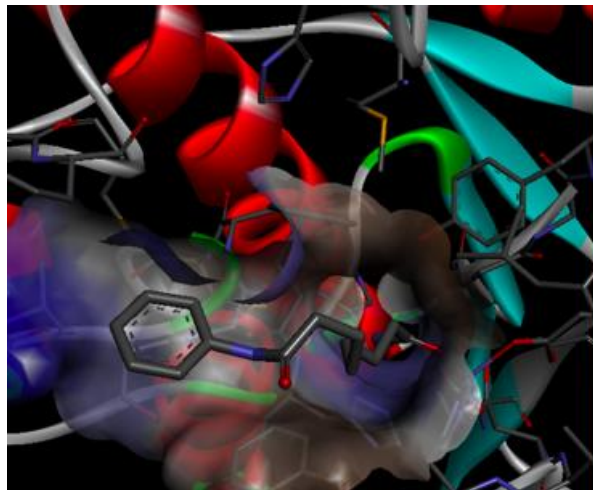
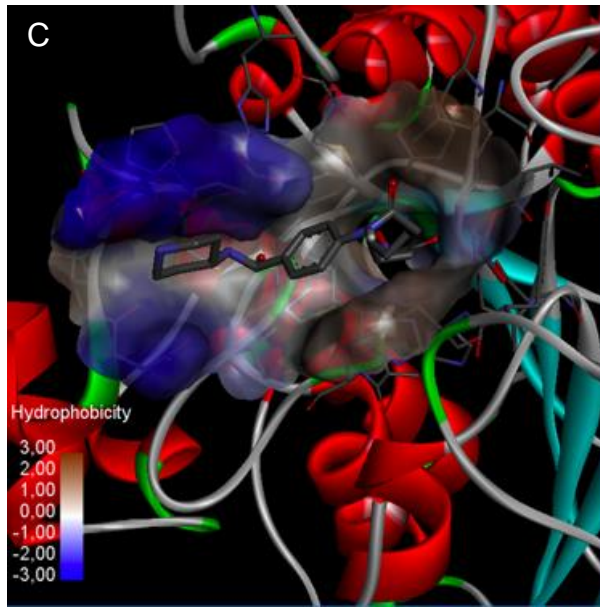
Additional molecular modelling data

Colour code:

Hydrophobicity is represented as a transparent cloud from brown to blue. Hydrogen bonds are represented as green dotted line when the distance is shorter than 3.4Å for an angle between acceptor and donor between 90° and 180°. π -Atom interactions correspond to hydrophobic interactions within a distance less than 3.5Å when the angle between the two interactants is less than 40°. They are shown as orange dashed lines for the π -anion interactions, purple dashed lines for π -sigma ones and pink dashed lines for alkyl bond ones. π - π stacking is shown as dark pink dashed line for interactants closer than 4.5Å with an angle lower than 25°. Grey dashed lines represent interactions between acceptors and zinc when the angle between the interactants is above 50° and the distance is less than 3.2Å. Unfavourable interactions are represented in red dashed line.

Supplementary Figure 1: Modelling of compounds **4**, **19** and SAHA within human HDAC1(PDB: 5ICN) active site and their related interactions. Transparent surrounding represents the hydrophobicity of the active site. Secondary structures are represented as ribbons with α -helix in red and β -sheets in blue. A) Compound **4** docked in the active site of HDAC1. B) 2D representation of the interaction in binding of **4** in HDAC1 catalytic pocket. C) Compound **19** docked in the active site of HDAC1. D) 2D representation of interactions of binding of **19** in HDAC1 catalytic pocket. E) SAHA docked in the active site of HDAC1. F) 2D representation of interactions of SAHA in HDAC1 catalytic pocket.





Supplementary Figure 2: Modelling of compounds **4**, **19** and SAHA in the catalytic site of human HDAC6 (PDB: 5EDU) and their related interactions. Transparent surrounding represents the hydrophobicity of the active site. Secondary structures are represented as ribbons with α -helix in red and β -sheets in blue. A) Compound **4** docked in the active site of HDAC6. B) 2D representation of the interactions of the binding of **4** in HDAC4 catalytic pocket. C) Compound **19** docked in the active site of HDAC6. D) 2D representation of interactions of the binding of **19** in HDAC4 catalytic pocket. E) SAHA docked in the active site of HDAC6. F) 2D representation of interactions of the binding of SAHA in HDAC4 catalytic pocket.

