

# Structure-activity relationships of new Schiff bases derived from diaminomaleonitrile as new agents for the treatment of Chagas disease

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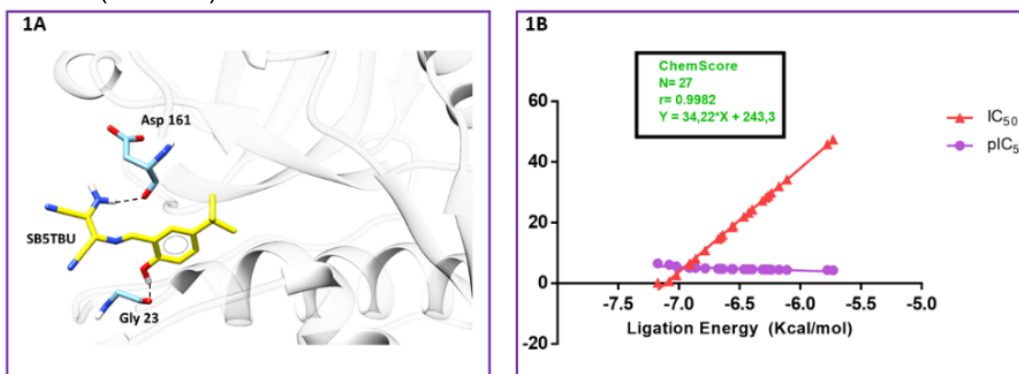
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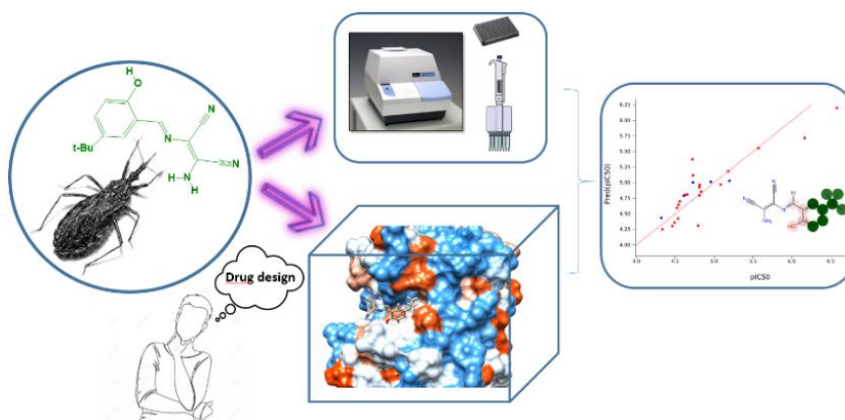
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## ABSTRACT

Schiff bases have attracted considerable attention from organic and medicinal chemists due to their drug-like properties. Here, we have synthesized 27 new Schiff bases derived from diaminomaleonitrile in high yields (80-98%) and excellent atomic economy (92-94%). Molecular docking using the cruzain structure (3KKU), demonstrated that the t-butyl group present in the most active compound (IC<sub>50</sub> = 0.263 μM) is fundamental to the establishment of two hydrogen bonds and to the inhibitory activity: one between the amino group from the ligand and the aspartic acid-161 residue and the other between the hydroxyl group and the glycine-23 residue (Figure 1A). A good correlation was observed between IC<sub>50</sub> values and binding energies (ChemScore function, Figure 1B). 2D QSAR models using a kernel-based partial least square regression method were subsequently developed to predict the cruzain inhibition. The resulting models showed R<sup>2</sup> = 0.79, Q<sup>2</sup> = 0.67 and a low standard deviation (SD < 0.4).



## GRAPHICAL ABSTRACT



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## REFERENCES

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