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2D QSAR Studies on a Series of Fenarimol Derivatives with Trypanocidal Activity

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Highlights

A robust and predictive Hologram Quantitative Structure-Activity Relationship (HQSAR) model was developed for a series of 52 fenarimol derivatives with anti-*Trypanosoma cruzi* activity.

Abstract

Chagas disease affects 8 million people worldwide, mostly in Latin America, causing more than 10,000 deaths per year and putting at risk of infection more than 25 million people. Pharmacotherapy of Chagas disease is restricted to a few options whose inefficacy and associated adverse effects demonstrate the urgent need for novel, safe and effective drugs.[1] 2D quantitative structure-activity relationship (QSAR) models were developed for a series of fenarimol derivatives with trypanocidal activity, using the Hologram Quantitative Structure-Activity Relationship (HQSAR) method. The data set consists of 52 molecules collected from the literature, for which IC_{50} values against *Trypanosoma cruzi* were determined.[2] The final HQSAR model, based on molecular fragments of 4-7 atoms and A/B/C/H/Ch fragment distinction, showed appropriate statistical consistency (r^2 = 0.96 and q^2 = 0.66) and predictive ability for test set compounds (r^2_{pred} = 0.66). The 2D contribution maps indicated key structural features most closely related with the biological activity (Figure 1). These findings demonstrate the usefulness of the HQSAR model to guide the design of novel trypanocidal agents structurally related with the investigated data set.

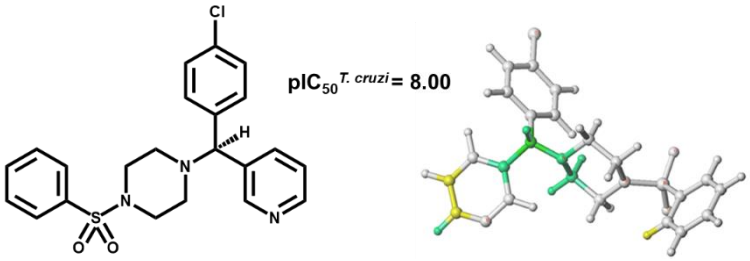

Figure 1. Structure, biological activity and HQSAR contribution map for a data set compound.

References

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