

Correlating biological activity with field patterns for histamine H3 antagonists

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Abstract

[TorchLite](#) is a free molecular editor and viewer that displays molecules in 2D or 3D with their associated field patterns and physicochemical properties. The following example shows the power of TorchLite to illuminate the relationship between field patterns and biological activity for histamine H3 antagonists.

Method

Histamine plays a variety of physiological roles in the CNS and peripheral tissues through the four known G protein-coupled receptors, H1, H2, H3, and H4¹. Histamine H3 receptor antagonist-enhanced neurotransmitter release offers a promising approach to the treatment of several CNS disorders².

TorchLite is a molecular editor and viewer that displays molecules in 2D or 3D with their associated field patterns and physicochemical properties. It can be used to analyze activity, toxicity and ADME properties and correlate them with molecular fields.

Data on several H3 antagonists were extracted from ChEMBL³ and analyzed with TorchLite. Each member of the chemical series was drawn in TorchLite and molecular fields added (figure 1). The field point patterns were studied to delineate the root causes of biological activity.

Higher activity was associated with negative field patterns in the lower left of the presented molecule views, and was probably due to specific hydrogen bonding interactions. However, the highest actives also presented high electron density in both the terminal and central 6,5 aromatic ring systems, as evidenced by larger negative molecular surfaces shown in figure 2.



Figure 1: A series of H3 antagonists displayed in TorchLite, showing the 2D structure and the aligned, minimized 3D conformation. The molecular field patterns are shown as coloured spheres. TorchLite's flexible interface lets you view molecules side by side, superimposed or as a list.

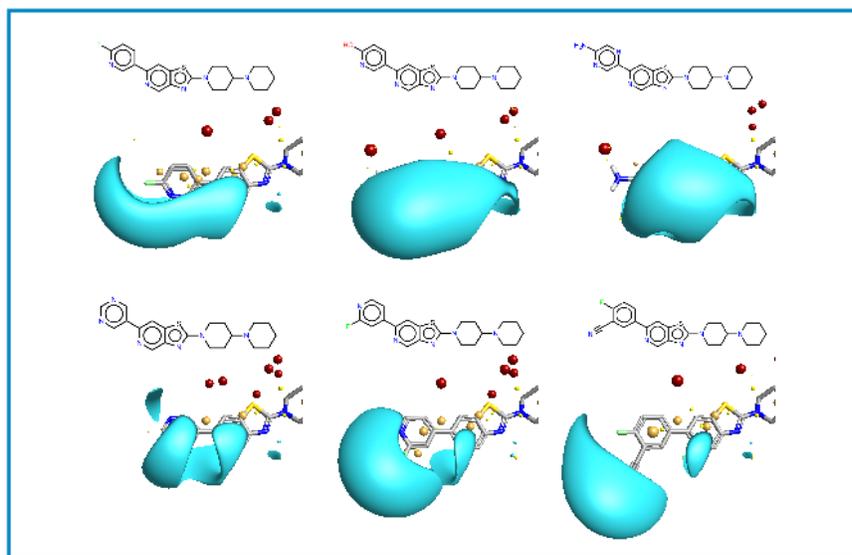


Figure 2: The molecules with the greatest activity presented high electron density in both the terminal and central 6,5 aromatic ring systems, as evidenced by larger negative molecular surfaces.

Conclusion

This analysis shows the correlation between biological activity and field patterns, and demonstrates the power of the field technology in TorchLite.

TorchLite is available free from: www.cresset-group.com/product/torchlite

References

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2. M. Berlin and C. Boyce, 'Recent advances in the development of histamine H3 antagonists', Expert Opin. Ther. Patents (2007) 17(6), 675
3. Available from EBI at <https://www.ebi.ac.uk/chembl/db/>