Atomic-Scale Insights into the Interaction of Cobaltabis(dicarbollide) with DNA: A Molecular Modelling Perspective

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Boron neutron capture therapy (BNCT) is an emerging cancer treatment strategy that relies on boron-containing agents to selectively target tumor cells. Cobaltabis(dicarbollide) ([COSAN]$^-$), a metallacarborane complex with a high boron content, is a promising candidate for BNCT. However, its interaction with nucleic acids, a key determinant of its therapeutic potential, remains controversial.

In this work, we employ a multiscale molecular modelling approach, integrating microsecond long molecular dynamics (MD) simulations, hybrid quantum mechanics/molecular mechanics (QM/MM) calculations, and binding free energy estimations, to resolve the binding mechanism of [COSAN]$^-$ with DNA at an atomic level.

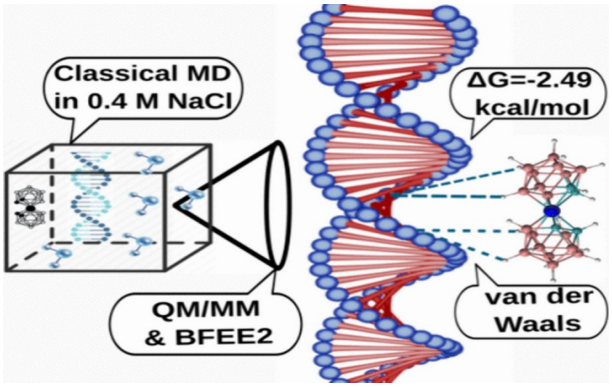

Figure 1: Atomic-scale insights into [COSAN]$^-$ interactions with DNA from MD and QM/MM simulations, revealing weak binding energetics.

Our findings reveal that [COSAN]$^-$ interacts weakly with DNA, preferentially binding to the major groove via dihydrogen B–H· · ·H–N bonding [1]. Moreover, our results demonstrate a strong dependence on ionic strength, with binding events observed primarily at high NaCl concentrations. These insights contribute to a fundamental understanding of metallacarborane interactions with biomolecules and provide a molecular basis for designing improved boron delivery systems for BNCT

[1] D. Halder, A. M. A. Abdelgawwad, and A. F. Monerris, *J. Med. Chem.*, **2024,** 67(20), 18194-18203.