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THEORETICAL AND *IN SILICO* ANALYSIS OF MOLECULAR INTERACTION OF ANTI-TRYPANOSOMAL DRUG BERENIL AND ITS ANALOG WITH CALF THYMUS DNA

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ABSTRACT : Several studies suggested that Berenil, an anti-trypanosomal drug, acting as minor groove binders intercalates with DNA subsequently providing thermal stabilization to the drug-DNA complex. In the present study, we theoretically analyzed Berenil binding with calf thymus DNA using experimental models of De-Abreu *et al* (2008) to explain the melting behaviour and heat capacity of DNA in the presence and absence of Berenil. Drug-DNA complex were also analyzed for the interactions and binding energy of the docked structure through *in silico* analysis. Using modified Zimm and Bragg theory the sharpness of transition was examined in terms of half width and sensitivity parameter ($\Delta H/\sigma$). The molecular docking technique was adopted to find out the binding affinity of Berenil and its derivatives with DNA. All obtained conformations of drug-DNA complex were analyzed for the interactions and binding energy of the docked structure using Discovery Studio.

The results of theoretical analysis concluded that the various parameters such as heat capacity curve, transition profile, half widths and sharpness of the transition are in good agreement with the experimental measurements for binding of Berenil determined through *Differential Scanning Calorimetry (DSC)*. Molecular docking studies of Berenil and its analog N-(3-hydroxypropyl)-Berenil (NHB) using Accelrys Discovery studio client 4.1 further confirmed that Berenil exhibited better binding parameters in terms of higher binding energy with lower inhibition constant compared to the NHB. Theoretical analysis proposed in this study in conjunction with *in silico* tools could provide a reliable approach to design potential therapeutic DNA binding agents and understand their interaction.

Key words : Berenil, DNA binding, transition profile, heat capacity, *in silico*.