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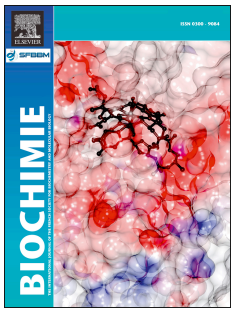

Biophysical and *in silico* interaction studies of aporphine alkaloids with Malonyl-CoA: ACP transacylase (FabD) from drug resistant *Moraxella catarrhalis*

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Abstract

Malonyl-CoA:acyl carrier protein transacylase (FabD), being an essential enzyme of the FAS II pathway, is an attractive target for developing broad-spectrum antibiotics. It performs initiation reaction to form malonyl-ACP, which is a key building block in fatty acid biosynthesis. In this study, we have characterized the FabD from drug-resistant pathogen *Moraxella catarrhalis* (McFabD). More importantly, we have shown the binding of McFabD with three new compounds from the class of aporphine alkaloids. ITC based binding studies have shown that apomorphine is binding to McFabD with a stronger affinity (K_D = 4.87 μM) as compared to boldine (K_D = 7.19 μM) and magnoflorine (K_D = 11.7 μM). The possible mechanism of fluorescence quenching is found to be static with K_q values higher than 10^{10}, which was associated with the ground state complex formation of aporphine alkaloids with McFabD. Conformational changes observed in the secondary and tertiary structure marked by the loss of helical content during the course of interactions. Molecular docking based studies have predicted the binding mode of aporphine alkaloids and it is found that these compounds are interacting in a similar fashion as known inhibitor corytuberine is interacting with McFabD. The analysis of docking poses have revealed that His 210, Leu102, Gln19, Ser101 and Arg 126 are critical residues which may play important role in binding. The growth inhibition assay has shown that apomorphine has better MIC value (4-8 μg/ml) against *Moraxella catarrhalis* as compared to boldine and magnoflorine. Therefore, the current study suggests that aporphine alkaloids can act as antibacterial agents and possible target of these compounds could be FabD enzyme from the FAS II pathway, and apomorphine scaffold will be more suitable among these compounds for potential development of antibacterial agents.