Parasitic diseases cause major morbidity and mortality throughout the globe. Specific activation of amino acids by aminoacyl-tRNA synthetases (aaRSs) is essential for maintaining fidelity during protein translation. Therefore, small molecule targeting of aaRS active sites is an attractive avenue from the perspective of developing anti-infectives. In recent years, several aminoacyl-tRNA synthetases (aaRSs) have been validated as drug targets for parasitic diseases. Febrifugine and its derivatives like halofuginone are known to inhibit the prolyl-tRNA synthetase (PRS). We have determined the parasitic PRS enzyme in complex with febrifugine derivatives. The two monomers that constitute dimeric PRS display significantly different conformations in their active site regions. Co-crystallisation experiments led to a new crystal form in some cases. Here we describe the structural comparison of inhibitors bound to parasitic PRSs, and investigate the binding modes of these inhibitors.

**Keywords:** Infection, PRS, Inhibitor