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Crystal structure of the bacterial protein HemS in complex with haem

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Iron is one of the most important nutrients for the majority of living organisms due to its essential role in many biological processes like respiration and oxygen transport. Despite being one the most abundant chemical elements, iron is scarcely available under physiological conditions, because of its insolubility and toxicity.
Pathogenic bacteria rely on their host as source of iron and have evolved several strategies to circumvent their iron dependency. One mechanism relies on ''stealing'' iron in the form of haem from host's haem proteins through a set of inter-linked haem transporters [1]. These unique systems have intriguing molecular biology mechanisms.
The haem uptake system of the gastrointestinal pathogen *Yersinia enterocolitica* consists of 5 proteins. Located on the outer membrane, the receptor HemR sequesters haem from host haem proteins or directly binds free haem. When internalised, the ligand is taken up by the periplasmatic carrier HemT and passed onto the hetero-dimer HemUV, an integral inner membrane permease. In the cytosol, haem is bound and possibly degraded by the soluble protein HemS [1,2,3].
Structure-function relationship in the HemS molecule were studied through sequence alignments, site-directed mutagenesis of conserved residues possibly involved in haem-iron coordination and UV/Vis spectroscopy. These experiments identified histidine 196 as the ligand to the iron. Furthermore the structure of HemS in complex with haem was solved by molecular replacement with the homologues apo-protein structure from *E. coli* (ChuS [4]) and refined to 1.7 Å, revealing a novel haem-binding site.

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Hydrogen bonded hexagonal rings: effect on molecular geometry

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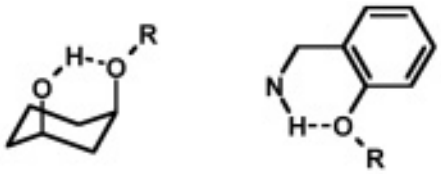
We report structures for two molecules of medicinal interest: an oxysterol containing motif **I** and an alkoxyphenyimidazo-1,3,5-triazine containing **II**. As shown, both molecules form intramolecular hydrogen bonds with H ...O distances 1.93 and 1.94 Å respectively. The OH and NH groups do not interact with a carbonyl group elsewhere within each molecule that could accept an intermolecular hydrogen bond.



I II

This apparent preference for 6-membered rings prompted a search for other molecules matching these types in the Cambridge Structural Database. Application of the criteria used by Bilton et al. [1] ($R \leqslant 0.1$, no errors, not polymeric, only organics) with normalisation of terminal hydrogen atom positions yielded 596 hits of type **I** and 462 of type **II**. Elimination of molecules with cyclic and CCCN torsion angles that preclude hydrogen bonding reduced these numbers to 194 and 304. Histograms of the H ...O contact distance had minima near 2.8 Å, suggesting that it is suitable to designate as hydrogen bonds those contacts that do not exceed the 2.72 Å sum of the van der Waals radii [2]. In the two groups this procedure identified 147 and 234 molecules respectively as intramolecularly hydrogen bonded. Further restriction to ''strong'' hydrogen bonds (H ...O contact $\leqslant$ 2.30 Å for O-H ...O and 2.35 Å for N-H ...O [1]) left 124 and 188, i.e. just over 60% of the hits with permissive geometry. As expected in order to avoid like charges in proximity, the X-H ...O angle has a strong negative correlation with H ...O distance (coefficient < -0.86 for all intramolecular hydrogen bonds). Scattergrams of the X-H ...O-C torsion angle versus H ...O distance converge on torsion angles near zero for the shortest hydrogen bonds. Magnitudes of torsion angles across the ring from the hydrogen bond also tend to be smaller for the shortest hydrogen bonds. When a least-squares plane is defined by the six atoms of the hydrogen-bonded ring, their average deviation gives a correlation coefficient with the H ...O distance of 0.768 for the fairly rigid I and 0.874 for the more flexible II. From the evident association of flattened rings with short hydrogen bonds it is difficult to identify which is the cause and which is the consequence, but this tendency should be taken into consideration by molecular modellers.

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