Crystallization and structural studies of an aldo-keto reductase from opium poppy

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Many pharmaceuticals in use today are produced in plants via a plethora of specialized metabolic pathways. Benzylisoquinoline alkaloids (BIA) are a large and diverse group of pharmacologically active compounds found in a variety of plants, including the opium poppy. Among the most important BIAs are morphine and its immediate biosynthetic precursor codeine. In the poppy, codeine is reduced from codeinone by the enzyme codeinone reductase (COR). However, COR can catalyze alternative side-reactions that yield unwanted compounds, such as neopine. The accumulation of less desirable products from these side-reactions seriously compromises the efficiency of current synthetic biology efforts to develop fermentation-based production systems in yeast and bacteria. To understand the molecular structural mechanisms responsible for substrate recognition, and to inform protein engineering and systems biology efforts to minimalize unwanted alternate reactions, we have crystallized COR and measured diffraction data to 2.9 Å resolution (completeness 99.5%, R_{sym}=0.135, redundancy=10.5). Molecular replacement calculations using chalcone reductase (52% sequence identity) as a search model indicate three copies in the asymmetric unit (space group $P3_121$; a=87.5 Å, b=87.5 Å, c=221.0 Å; 44.6% solvent). Additional work in the co-crystallization of complexes with substrates and cofactors is currently under way.