Crystallization and preliminary structural studies of an aldo-keto reductase from Opium Poppy

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Plants are still the source of many widely used pharmaceuticals produced 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 plants, codeine is reduced from codeinone by the enzyme codeinone reductase (COR). However, COR also catalyzes alternative reactions that yield unwanted compounds, such as neopine. These unwanted compounds are a problem in recent attempts at establishing fermentation-based production systems in yeast and bacteria. To understand the molecular structural mechanisms responsible for substrate recognition, and to inform protein engineering efforts to minimalize unwanted alternate reactions, we have crystallized COR and measured diffraction data to 2.7Å resolution. The symmetry in the diffraction pattern and systematic absences suggest that the space group is most likely either $P6_222$ or $P6_422$, with unit cell parameters a=b=87.3Å, c=219.0 Å. The optimization of crystal quality, cocrystallization of complexes with substrates and substrate analogues/inhibitors, and structure determination using molecular replacement and SAD phasing, are currently in progress.