in the molecule. This probably contributes to the activity expression of the present psychrophic enzyme at low temperatures.

Keywords: biological macromolecules, dehydrogenases, cold adapted enzymes

**P04.02.82**

*Acta Cryst.* (2008). A64, C256

Crystallographic analysis of complexes of bovine trypsin and Schiff base metal chelate

Susumu Kawano, Daisuke Iyaguchi, Midori Tateyama, Eiko Toyota

Health Science University of Hokkaido, Faculty of Pharmaceutical Sciences, kanazawa 1757, Ishikari-Tobetsu, Hokkaido, 061-0293, Japan, E-mail: s.kawano@hoku-riyo-u.ac.jp

Studies on trypsin-specific compound are useful for the design of clinical useful compounds, since a variety of physiologically important enzymes (e.g. thrombin, kallikrein and urokinase) have trypsin-like specificity. Several benzamidine and phenylguanidine derivative have been reported to be potent inhibitor. In our previous papers, we have reported of the Schiff base copper(II) chelates carrying a guanidinium group. The chelates are strong inhibitor of trypsin (K \(_i\) = \(10^{-5}\) M). To elucidate the structure-activity relationship in this novel series of inhibitors, the crystal structure of complexes between trypsin and guanidine-containing inhibitors were determined. The crystals (1.2) were obtained by equilibrating the droplet containing 1.25 mM trypsin, 0.1 M Tris-HCl buffer (pH 8.0), 22\% (v/v) PEG 4000 and 0.2 M lithium sulfate. Guanidinium group of crystal I forms hydrogen bonds with Asp180Glu\(_2\), Ser190Glu\(_1\), and Gly2190. The copper(II) ion of inhibitor is in close contact with His57 and Ser195. The imidazole nitrogen of His57 is directly coordinated with the copper(II) ion (2.33 Å). The copper(II) ion coordinated by the imine nitrogen, the phenolic oxygen and one carboxyl oxygen of the Schiff base ligand. In conjunction with detailed structural analysis, this approach will hopefully lead to the development of more potent inhibitor specifically targeting trypsin-like protease, as well as other physiologically important enzymes.

Keywords: X-ray crystallography of proteins, enzyme inhibitor design, medicinal chemistry

**P04.02.84**

*Acta Cryst.* (2008). A64, C256

Structural biology study in biosynthesis of plant natural products

Xiaojiang Wang, Lenong Li, Hui Shao, Luis L. Escamilla-Trevino, Zhenzhao Chang, Luzia Modolo, Jack W. Blount, Xianzhi He, Richard A. Dixon, Zhiqiang Pan

1 The Samuel Roberts Noble Foundation, Plant Biology Division, 2510 Sam Noble Parkway, Ardmore, Oklahoma, 73401, USA, 2 Natural Products Research Center, University of Mississippi, University, MS 38677, E-mail: xwang@noble.org

Plants may be regarded as biofactories and synthesize over 200,000 natural products. Many of plant natural products can be used for the benefit of human and animal health. The biosynthesis of plant natural products is a very complex process including many different chemical reactions. We are working on three types of enzymes important for plant natural product biosynthesis, glycosyltransferases involved in glycosylation reactions, reductases involved in reductions, and cytochrome P450s involved in hydroxylation and dehydration. We determined crystal structures of several uridine diphosphate glycosyltransferases, NADPH-dependent reductases, and a cytochrome P450 enzyme. These structures provide essential insights into their structure-function relationships and catalytic mechanisms in the complex biosynthetic processes. Structure-based mutagenesis and the further functional study help to explore the roles of key residues for catalysis and specificity, and decipher the mechanisms. These studies may also provide us the basis for in vitro manipulation of enzyme activity and substrate specificity, and further rationally-based metabolic engineering and manipulation.

Keywords: enzyme structure function, crystal structures, biosynthesis