FA1-MS03-P01

Primaquine and Chloroquine as Inhibitors for Human Quinone Reductase 2 Enzyme. Majed M. AbuKhader. *Faculty of Pharmacy, Philadelphia University, PO Box: 1, 19392 Amman, Jordan.*
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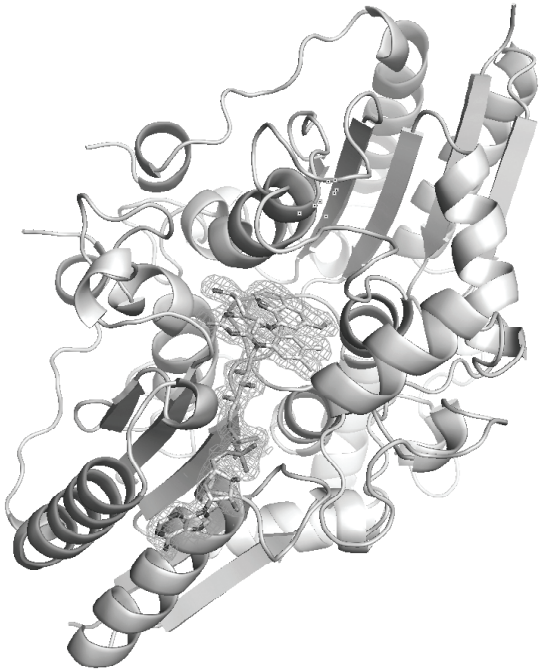
Quinoline-based drugs such as primaquine and chloroquine are pupolar antimalaria drugs. In addition to their action on malaria parasite, they show a variation in their inhibition property of quinone reductase 2 enzyme (NQO2) which is a dominant enzyme in erythrocyte [1, 2]. The inhibiton of this particular enzyme in erythrocyte suggests the accumulation of superoxide radicals which kill malaria parasite. Through structural studies at the atomic level using x-ray crystallography, it was possible to explain the inhibition properties for primaquine and chloroquine towards NQO2. Primaquine and chloroquine were co-crystallized with NQO2 and the crystal structures of these complexes were resolved at 1.65Å and 1.83Å respectively. These structures illustrated that primaquine is bound tightly in a compact manner with NQO2. This is due to the presence of polar as well as hydrophobic interactions with amino acids of NQO2 active site. In case of chloroquine, the complex structure suggests a very weak binding with only hydrophobic interaction. The results explain the reason behind the strong and weak inhibition ability for primaquine and chloroquine towards NQO2 respectively. The information presented in this work could be further exploited in drug design studies to develop new possible antimalaria agents.



[1] Graves P.R., Kwiek J. J., Fadden P., Ray R., Hardeman K., Coley A. M., Foley M., Haystead T. A., *Mol. Pharmacol.*, **2002**, 62(6), 1364-1372. [2] Kwiek J.J., Haystead T. A., Rudolph J., *Biochemistry*, **2004**, 43, 4538-4547.

Keywords: quinonr reductase2; primaquine; chloroquine; antimalaria drugs

FA1-MS03-P02

A Structural Basis for the pH-Dependant Xanthophyll Cycle. Pascal Arnoux[a], Tomas Morosinotto[b], Giorgia Saga[b,c], Roberto Bassi[c], David Pignol[a]. [a]*Laboratoire de Bioénergétique Cellulaire, Saint-Paul-lez-Durance, 13108, France.* [b]*Università degli studi di Padova, Padova, Italy.* [c]*Università degli studi di Verona, Verona, Italy.*
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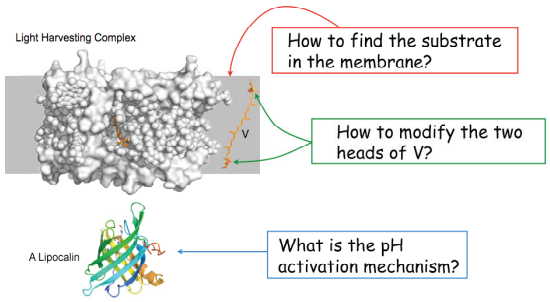
Plants adjust their photosynthetic activity to changing light conditions. A central regulation is the xanthophyll cycle in which the carotenoid violaxanthin (V) is converted into zeaxanthin (Z) in strong light, with the dissipation of the excess absorbed energy as heat and the scavenging of reactive oxygen species. Violaxanthin de-epoxidase (VDE), the enzyme responsible for Z synthesis, is activated when the thylakoid lumen becomes acidified as a result of high photosynthetic activity: at neutral pH VDE is a soluble and inactive enzyme whereas it attaches to the membrane with a marked cooperativity at acidic pH. VDE also uses ascorbate as a co-substrate with a pH-dependent K_m that may reflect a preference for ascorbic acid.
We determined the structures of the central lipocalin domain of VDE (VDE_{cd}) at acidic and neutral pH. At neutral pH, VDE_{cd} is monomeric with its active site occluded in a lipocalin barrel. Upon acidification, the barrel opens up and the enzyme appears as a dimer. The channel linking the two active sites of the dimer can harbour the entire carotenoid substrate and thus may permit the parallel de-epoxidation of the two violaxanthin β-ionone rings, making VDE an elegant example of the adaptation of an asymmetric enzyme to its symmetric substrate.



Keywords: photosynthetic proteins; membrane protein; regulation and reaction mechanisms of enzymes

FA1-MS03-P03

The Structure of DapD from *Mycobacterium Tuberculosis.* Linda Schuldt[a], Simone Weyand[a], Georgia Kefala[a], Manfred S. Weiss[a]. [a]*EMBL Hamburg Outstation, c/o DESY, Notkestraße 85, D-22603 Hamburg, Germany.*
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Tuberculosis (TB) is a bacterial infectious disease predominantly caused by the pathogenic bacterium