X-ray Crystallograpy of the Antiepileptic Drug Zonisamide with CA II

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Zonisamide, **ZNS**, is a widely used antiepileptic drug [1] whose mechanism of action is still not fully clarified. Recently a patent[2]claimed that ZNS is also effective for reducing weight in obese subjects and for treating eating disorders.

In a previous study we showed by means of solution and X-ray studies, that another sulfonamidic antiepileptic drug, Topiramate, is a strong inhibitor of physiologically relevant human carbonic anhydrase (hCA) [3]. Thus we decided to investigate the interaction of ZNS with the CA isozymes involved in lipogenesis and other metabolic processes, through the crystallographic analysis. Here we report the X-ray crystal structure of the complex ZNS-hCA II at a resolution of 1.70 Å, showing that the ZNS participates in the classical inhibitory interactions with the Zn(II) ion and with specific residues in the active site of the hCA II.

Thus the activity of this drug in different metabolic pathways must be reconsidered also according to its possibility of interaction with different CAs.

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