

Substrate Promiscuity of Methionine Gamma Lyase Deaminase from *Porphyromonas gingivalis*: Characterization by UV-VIS Spectroscopy

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Methionine Gamma Lyase Deaminase (Mgld) is a pyridoxal phosphate (PLP) dependent enzyme that cleaves L-methionine into methylthiol and forms the deaminated product alpha-ketobutyrate. Cloned, Overexpressed, Mgld was purified by affinity, gel filtration and DEAE ion exchange chromatography [1]. Purified Mgld was used for characterization of therapeutic use [2] and for enzyme kinetic studies [3]. D-methionine is slow in reactivity relative to L-isomer. Thus, the stereo selectivity is not perfected by Mgld. The thio ether bond is not a mandatory requirement for cleavage, since cysteine and homocysteine that has thiol group, can be cleaved into hydrogen sulfide and forms the corresponding deaminated, keto acid products pyruvate and alpha-ketobutyrate. Alpha-methyl DL-methionine is not a substrate due to steric hindrance that prohibits external aldimine formation with the Mgld-PLP. N-formyl and N-acetyl methionine are not substrate for Mgld, which makes sense, since the alpha-amino group is mandatory for binding as well as external aldimine Schiff's base formation. Thus, F-met or protein modified N-acetyl-met formation is a mechanism by which organisms have managed to protect methionine from degradation and keeps the modified methionine strictly for anabolic purposes. Serine and homoserine are weak substrates for Mgld which means sulfur to oxy substitution can be tolerated to certain degree for cleavage. L-methionine sulfone and L-sulfoxy methionine are sulfur modifications of the methionine, and Mgld exhibits higher K_m and a change in K_{cat} making the overall catalytic efficiency (K_{cat}/K_m) lower compared to L-methionine. Mgld is a good model system for structure/function studies of coenzyme mediated tight active site catalysis.

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[1]. D. Morcos, B.J. Schmier, A. Malhotra, K.V. Venkatachalam, *Biochem Anal Biochem* **2015**, 4:4- 1000223-1000229.

[2]. P.A. Faria, H.L. Laubach, K.V. Venkatachalam, *J Genet Syndr and Gene Ther*, **2013**, 4:1, 1000125-1000130.

[3]. T.C. Foo, A.C. Terentis, K.V. Venkatachalam, *Anal Biochem*, **2016**, 507, 21-26.