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Tryptophan and Its Derivative Oxidation by Heme-Dioxygenase Enzyme

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Abstract : Tryptophan oxidation by Heme-dioxygenase enzyme is initial important stepTryptophan oxidation by Heme-dioxygenase enzyme is initial important step in kynurenine pathway implicating to several severe diseases such as Parkinson's Disease, Huntington Disease, poliomyelitis and cataract. It is crucial to comprehend the oxidation mechanism with the hope to find decent treatment upon abovementioned diseases. The mechanism has been debatable since no one has been yet proved the mechanism obviously. In this research we have attempted to prove mechanistic steps of tryptophan oxidation via human indoleamine dioxygenase (h-IDO) using various substrates: L-tryptophan, L-tryptophan (indole-ring-2-13C), L-fully-labelled13C-tryptophan, L-N-methyl-tryptophan, L-tryptophan and 2-amino-3-(benzo(b)thiophene-3-yl) propanoic acid. All enzyme assay experiments were measured using a UV-Vis spectrophotometer, LC-MS, 1H-NMR, and HSQC. We also successfully synthesized enzyme products as our control in NMR measurements. The result exhibited that the distinct substrates produced N-formyl kynurenine (NFK) and hydroxypyrrolloindoleamine carboxylate acid (HPIC) in different concentrations and isomers, correlated to the proposal of considered mechanism reaction in kynurenine pathway implicating to several severe diseases such as Parkinson's Disease, Huntington Disease, poliomyelitis and cataract. It is crucial to comprehend the oxidation mechanism with the hope to find decent treatment for the abovementioned diseases. The mechanism has been debatable since no one has yet proven the mechanism obviously. In this research we have attempted to prove mechanistic steps of tryptophan oxidation via human indoleamine dioxygenase (h-IDO) using various substrates: L-tryptophan, L-tryptophan (indole-ring-2-13C), L-fully-labelled13C-tryptophan, L-N-methyl-tryptophan, L-tryptophan and 2-amino-3-(benzo(b)thiophene-3-yl) propanoic acid. All enzyme assay experiments were measured using a UV-Vis spectrophotometer, LC-MS, 1H-NMR and HSQC. We also successfully synthesized enzyme products as our control in NMR measurements. The result exhibited that the distinct substrates produced N-formyl kynurenine (NFK) and hydroxypyrrolloindoleamine carboxylate acid (HPIC) in different concentrations and isomers, correlated to the proposal of considered mechanism reaction.

Keywords : heme-dioxygenase enzyme, tryptophan oxidation, kynurenine pathway, n-formyl kynurenine
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