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Explicable Enzymatic Mechanism of H-Ido to Oxidise Tryptophan by Employing Various Substrates

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Abstract : The study of dioxygenase enzymatic mechanism on tryptophan oxidation has been a wide interest since the reaction is rate-limiting step of kynurenine pathway. In this research, observation of tryptophan oxidation through h-IDO enzyme along with synthesis of enzyme products was conducted in order to comprehend how the enzyme works on distinct substrates. UV-vis spectrophotometry, LC-MS, H-NMR and HSQC measurement were carried out to characterise enzyme product. It is found that while tryptophan was oxidised to form Nformylkynurenine (NFK) as a major product and hydroxypyrroloindole amine carboxylic acid (HPIC) in cis and trans confirmed in HSQC, N-methyl tryptophan substrate was converted to NFK and trans HPIC only. Other intriguing results showed that 5-hydroxy- tryptophan and Stryptophan was degraded to become NFK and epoxide cyclic respectively. The formation of NFK was considered through dioxygenation pathway, however HPIC was formed via monooxygenation. The epoxide cyclic—considered as intermediate compound in the mechanism— from S-tryptophan was not able to cleave the epoxide ring since bond energy of epoxide was probably much stronger. This validates the enzymatic mechanism where the intermediate compound in the enzymatic mechanism is epoxide cyclic.

Keywords : tryptophan oxidation, heme-dioxygenases, N-formylkynurenine, hydroxypyrrroloindoleamine, monooxidation
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