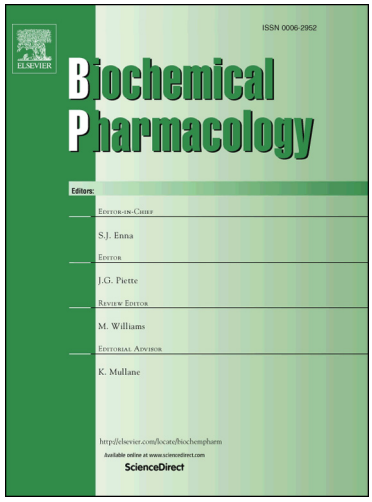
Accepted Manuscript



The two faces of aldehyde oxidase: oxidative and reductive transformations of 5-nitroquinoline

Erickson M. Paragas, Sara C. Humphreys, Joshua Min, Carolyn A. Joswig-Jones, Jeffrey P. Jones

PII: S0006-2952(17)30565-8
DOI: http://dx.doi.org/10.1016/j.bcp.2017.09.002
Reference: BCP 12913

To appear in: *Biochemical Pharmacology*

Received Date: 1 August 2017
Accepted Date: 5 September 2017

Please cite this article as: E.M. Paragas, S.C. Humphreys, J. Min, C.A. Joswig-Jones, J.P. Jones, The two faces of aldehyde oxidase: oxidative and reductive transformations of 5-nitroquinoline, *Biochemical Pharmacology* (2017), doi: http://dx.doi.org/10.1016/j.bcp.2017.09.002

The two faces of aldehyde oxidase: oxidative and reductive transformations of 5-nitroquinoline

Erickson M. Paragas, Sara C. Humphreys, Joshua Min, Carolyn A. Joswig-Jones and Jeffrey P. Jones*

Department of Chemistry, Washington State University, Pullman, WA 99164

*Corresponding author: E-mail address: jpj@wsu.edu

Abstract:

Aldehyde oxidase (AOX) is a cytosolic enzyme responsible for the metabolism of some drugs and drug candidates. AOX catalyzes the oxidative hydroxylation of substrates including several aliphatic and aromatic aldehydes, and nitrogen-containing heterocyclic compounds. AOX is also reported to catalyze the reductive metabolism of nitro-compounds, *N*-oxides, sulfoxides, isoxazoles, isothiazoles, nitrite and hydroxamic acids. These reductive transformations are not well understood and are generally believed to only occur at low oxygen concentrations. In this study, we used 5-nitroquinoline (5NQ) as a substrate to further understand both the oxidative and the reductive transformations catalyzed by AOX. *In vitro* reaction of 5NQ with AOX under aerobic conditions generated the oxidized (2-oxo-5-nitroquinoline, 2-oxo-5NQ), the reduced (5-aminoquinoline, 5AQ) and the oxidized/reduced (2-oxo-5-aminoquinoline, 2-oxo-5AQ) metabolites. Interestingly, in human liver cytosol, co-incubation of 5NQ and known AOX oxidative substrates DACA and phthalazine significantly increased the yield of the reduced