INVESTIGATION OF THE KINETICS AND MECHANISM OF INACTIVATION OF PTP-SHP2 BY PEROXYCARBONATE AND PHYTOCHEMICALS

Sarah Marie Lewis

Dr. Kent Gates, Thesis Supervisor

ABSTRACT

Protein tyrosine phosphatases (PTPs) have a catalytic cysteine in their active site, and have a phosphor-enzyme intermediate. PTPs work in tandem with protein kinases in order to regulate many cellular signaling pathways. Due to the importance of control of these pathways, much attention has been given to PTPs.

Phytochemicals are compounds found in fruits and vegetables and have been used to treat many aliments. Isosthiocyanates (ITCs) are part of a subgroup of phytochemicals. Investigation into the mechanism of action for these compounds is important to understand how they are utilized within the cell. Due to ITCs ability to undergo nucleophilic attack by thiols, it was determined that ITCs show a time- and concentration-dependent inactivation of PTP-Src homology 2 (SHP2).

Hydrogen peroxide shows time- and concentration-dependent inactivation of PTP-SHP2. Studying the natural buffer system of the cell is important to decipher a PTPs ability to be oxidized at a rate quicker than that previously determined by hydrogen peroxide. Examination of the formation of a more reactive oxidant, and its ability to inactivate PTPs was performed. It was determined that the addition of bicarbonate increases the rate of inactivation of PTP-SHP2 roughly 10 fold, but this does not account for the rapid inactivation that is observed within a cell.