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Zhiwei Liu  
*University of Massachusetts Dartmouth*

Maolin Guo  
*University of Massachusetts Dartmouth*, mguo@umassd.edu

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Inhibition of protein tyrosine phosphatase 1B by polyphenol natural products: relevant to diabetes management

Zhiwei Liu and Maolin Guo (email: mguo@umassd.edu)

UMass Cranberry Health Research Center; Department of Chemistry and Biochemistry, University of Massachusetts Dartmouth, MA 02747 (email: mguo@umassd.edu)

Many biologically active polyphenols have been recognized for their beneficial effects in managing diabetes and their complications. However, the mechanisms behind their functions are poorly understood. As protein-tyrosine phosphatase 1B (PTP1B) has been identified as a target for anti-diabetic agents, the potential inhibitory effects of a dozen structurally diverse polyphenol natural products have been investigated. Among these polyphenols, potent inhibitory activities have been identified for 6 of them with IC₅₀ in micromolar range, while the other polyphenols showed very weak inhibition. A structure-activity relationship (SAR) study and molecular docking results suggest that both a rigid planar 3-ring backbone and appropriate substitutions of hydroxyl groups benefit the inhibitory activity. The mechanism of inhibition of PTP1B was further investigated by Michaelis-Menten kinetics and the inhibition mode for PTP1B was determined along with the inhibition constant.