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Carbonic anhydrase: A new therapeutic target for managing Diabetes

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Background: Carbonic Anhydrase (CA) is a zinc metallo-enzyme that is critical to acid-base homeostasis. Carbonic anhydrase (CA) plays a fundamental role in the regulation of systemic acid-base homeostasis by facilitating urinary acidification. Inhibition of carbonic anhydrase results in acidification of the blood, leading to the manifestation of acidosis which is known to occur in diabetic subjects. The consequence is a decrease in pH that leads to loss of function of many enzymes and proteins.

Results: Here we report that 21 days after intraperitoneal injection of streptozotocin (STZ) 60 mg/kg body weight, there is a significant increase in carbonic anhydrase activity compared to control rats that received only vehicle. Correlation studies showed that carbonic anhydrase is negatively correlated with lactate level in the STZ induced diabetic rat model. In a second experiment a standard carbonic anhydrase inhibitor (acetazolamide) was given to (STZ 60 mg/kg body weight induced) diabetic rat model for a period of 28 days. The results showed a decrease in carbonic anhydrase activity with a marked rise in lactate level. A negative correlation was also seen between carbonic anhydrase activity and lactate level.

Conclusions: Here we have identified carbonic anhydrase activity to be altered in different stages of Diabetes Mellitus and its association with lactic acid as a response to high glucose level in the blood. Here we report that mild extracellular acidosis; a physiological consequence of lactic acid accumulation was due to high activity of carbonic anhydrase to preserve optimal pH of the blood by efficient secretion of H^+. Our findings suggest that inhibition of carbonic anhydrase in Diabetes results in lactic acid accumulation which ultimately leads to decrease in pH and results in cellular dysfunction.

Biography

Salihu Ibrahim Ismail is a Lecturer at the College of Medicine and Allied Health professions, Federal University Dutse. He received his BSc and MSc in Biochemistry from Bayero University Kano, and is completing a PhD in Biochemistry at Ahmadu Bello University, Zaria. His field of study includes metabolic profiling and metabolic diseases with special interest in diabetic complications. His research interest has focused primarily on identification of a prognostic biomarker for diabetic complications that could be used as therapeutic drug target.

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