Abstract

The main objectives of the thesis were to address three fundamental questions viz., (a) the impact of organophosphorous insecticides (OPI) in pancreatic dysfunction and ensuing hyperglycemia and the mechanism/s involved (b) the role played of OPI in inducing / exaggerating diabetic condition (c) dietary modulation of the OPI-induced hyperglycemia employing selected antioxidant phytochemicals. Our experimental approach involved biochemical studies employing both in vitro (rat pancreatic homogenate, isolated rat pancreatic islet culture, *C.elegans*) and in vivo (experimental rats) model systems. Initially we screened a few selected OPI for their toxicity and oxidative stress (OS) inducing potential. Results of our study revealed that OPI in general, Dimethoate (DM) and Dichlorvos (DDVP) in particular, have the potential to induce OS in vitro. Our results also clearly demonstrated that both DM and DDVP possessed the potential to alter blood glucose levels in rats, inhibit AChE and induce OS in pancreas. Altered glucose homeostasis induced by both DM and DDVP was associated with biochemical and oxidative impairments in pancreas as well as derangement in carbohydrate metabolism. Based on the results of our study, it could be surmised that rats pre-treated with OPI (DDVP) could be at a risk of developing diabetes if exposed to even a sub-diabetogenic dosage of a diabetogen (Streptozotocin). We also demonstrated that ‘epicatechin-rich’ ethanolic extract of cashew nut skin (CSE) is a powerful natural antioxidant and it had the propensity to offset DM and DDVP induced oxidative damage in rat pancreatic tissue *in vitro*. Our findings also established the ameliorative effect of CSE against OPI induced toxicity with special reference to pancreatic oxidative damage and altered glucose homeostasis in rats. In conclusion, the data obtained from the present series of investigations provide evidence on the effects of OPI on pancreatic dysfunction and their likely role in the development/ progression of metabolic disorder like diabetes. Our studies also demonstrated that OPI-induced pancreatic damage and hyperglycemia could be attenuated by antioxidant-rich phytochemicals.