CONCLUSIONS
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1. Of the selected OPI screened for their oxidative stress inducing potential in vitro, only ethion (ET), dimethoate (DM) and dichlorvos (DDVP) were found to enhance ROS generation, while only DDVP significantly increased lipid peroxidation in vitro. Both DM and DDVP were found to equitoxic to rat pancreatic islets and Caenorhabditis elegans.

2. An acute (oral) dose of DM (40 mg/kg b.w) elevated blood glucose levels significantly in adult male rats while, a single dose of DDVP (10 mg/kg b.w) failed to increase the blood glucose level to a significant extent. Interestingly, repeated oral doses of DDVP (10 or 20 mg/kg b.w /d for 5 or 10 d) induced a significant increase in blood glucose levels.

3. Repeated oral doses of Dimethoate (20 and 40 mg/kg b.w/d for 30 d) induced an elevation in blood glucose levels and also altered glucose tolerance in male rats. At these dosages, DM also induced marked oxidative stress in pancreas.

4. Elevated blood glucose levels in rats administered repeated oral doses of DDVP (20 mg/kg b.w /d for 10 d) was associated with significant perturbations in various biochemical markers in pancreas which are suggestive of pancreatic oxidative damage. Biochemical dysfunctions related to carbohydrate metabolism were also evident in DDVP treated rats.

5. Rats pre-treated with multiple oral doses of DDVP followed by a sub-diabetogenic dose of Streptozotocin showed much higher blood glucose and oxidative damage in pancreas in comparison with rats treated with DDVP or STZ alone suggesting that exposure to OPI can render the animal susceptible to diabetes.

6. Ethanolic extracts of novel plant-derived food processing wastes such as potato peel (PPE), tamarind seed coat (TSCE) and cashew nut skin (CSE)
varied in their yield and total polyphenolic content. Cashew nut skin yielded relatively higher extract with higher total polyphenols as compared to both potato peel and tamarind seed coat. All the extracts exhibited significant antioxidant activity *in vitro* in the different assay systems. However, CSE and TSCE were equipotent and their activity was comparable to that of BHA. HPLC analysis of the ‘antioxidant rich ethanolic extract of CSE’ showed epicatechin to be one of the major antioxidant components.

7. CSE and epicatechin significantly reduced the degree of ROS generated by DDVP *in vitro* in rat pancreatic homogenate while, β-carotene (1mM) failed to offer any protection. Both CSE and epicatechin effectively offset DDVP/ DM induced ROS generation in rat pancreatic islets *in vitro*.

8. Oral supplementation of rats with CSE had no appreciable effect on blood glucose levels. However, rats administered repeated oral doses of DDVP, along with CSE supplements, showed blood glucose levels, which were comparable to those of controls. The degree of pancreatic oxidative damage was also significantly attenuated in these rats.

9. In conclusion, the data obtained from the present series of investigations provide evidences on the effects of OPI on pancreatic function and their possible role in the development / progression of metabolic disorder like diabetes. Supportive evidences are also presented to demonstrate the involvement of oxidative stress in OPI induced pancreatic dysfunction and ensuing hyperglycemia. Our studies also demonstrate that OPI-induced pancreatic damage and hyperglycemia could be significantly abrogated by antioxidant-rich phytochemicals.

10. Thus, these studies suggest the potential of OPI in induction of diabetes in those who are occupationally exposed to OP pesticides (such as pesticides formulating employees or farmers who use OP pesticides) as well as the general public who may be exposed to OPI residues through food and water.