Abstract

The intestine is a major organ of the digestive system and is the primary site of exposure to nutrients/toxicants due to its extensive surface area and physiological properties. The intestine mucosal cell monolayer is also the first barrier regulating the entry of food components into the underlying tissues. Therefore, it is interesting to study the effect of chemicals or contaminants present in food that reach the gastrointestinal (GI) tract. GI disorders are on the increase globally although the etiological factors contributing towards most of the disorders of intestine are not known. The increased occurrence of pesticide residues in food and water, at levels beyond permissible limits, raises the concern regarding their contribution towards intestinal disorders.

The present work was carried out to (a) investigate the propensity of selected organophosphorus insecticides (OPI) to modulate functions of small intestine in normal rats (b) to study the interactive role of selected OPI and experimentally-induced diabetes on small intestine of rats (c) delineate the mechanisms by which the selected OPI modulates the structure and function of small intestine in normal rats.

The first set of studies clearly established the potential of two OPI - monocrotophos (MCP) and chlorpyrifos (CPF) to affect intestinal brush border enzymes and redox status in rats after multiple dosing. Of the two OPI, MCP was more potent in affecting intestinal functions (after 7d). Prolonged MCP treatment (30d) induced significant changes in small intestine compared to 7 and 15d treatment and these changes were evident in the jejunum (both structural and biochemical) compared to the other two intestinal regions. All the four disaccharidases, few dipeptidases, alkaline phosphatase, Na+, K+ ATPase showed increased activity. Alteration in the level and/or activity of redox state markers revealed the potency of MCP in inducing oxidative stress in the small intestine. Brush-border membrane lipid
composition and intestinal transit rate were also altered as a result of MCP treatment. In addition, several structural changes were also evident in the intestine of the treated rats. Kinetics of enzyme activation by MCP was studied in the intestinal brush border membrane isolated from rats treated with MCP for 30d. Regression analysis of the double reciprocal Lineweaver-Burk plot revealed that the $K_m$ (substrate affinity) of both sucrase and alkaline phosphatase remained unchanged in MCP treated rats, whereas $V_{max}$ recorded an increase.

The impact of repeated oral doses of MCP (for 15 and 30d) was also studied on the intestinal structure and functions in experimentally-induced diabetic rats wherein it was found to augment the structural and biochemical dysfunctions. Our results clearly demonstrate that intestine of diabetic rats are prone to further structural, functional and oxidative damage by MCP, which might result in exacerbated intestinal dysfunction. The current results appear to indicate the potential that long-term exposure to MCP residues may interfere with the digestive capacity of the small intestine and hence have long-term impact on human health.