AIM AND SCOPE OF THE PRESENT INVESTIGATION

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 intestinal epithelium constitutes one of the most important cellular membranes owing to its role in digestive and absorptive functions. The intestinal mucosa cell monolayer is also the first barrier that either allows or prevents the entry of food, toxins and pathogens, into the underlying tissues. Any alteration in the functional / structural features of the intestine can have tremendous impact on the overall health of the organisms since this could lead to an inadequate nutrient supply to the organism or result in certain disease pathology or aggravate any pre-existing disease pathology. Therefore, it is interesting to study the effect of chemicals or contaminants present in food that reach the gastrointestinal (GI) tract.

In recent times, gastrointestinal (GI) disorders are on the increasing globally. However, the etiological factors contributing towards most of the disorders of intestine such as, Crohn’s disease, irritable bowel syndrome, ulcerative colitis inflammatory bowel disease and GI bleeding are not clearly understood. Increased stress levels, altered food habits and environmental factors are speculated to play major roles. The increased occurrence of pesticide residues in food and water, at levels beyond permissible limits, raises the concern regarding their contribution towards intestinal disorders. Limited studies have been carried out to implicate the role of pesticides on intestinal dysfunctions. Very few organophosphorus insecticides (OPI) have been studied with regard to their potential to modulate functions and features of small intestine. OPI have been reported to be absorbed in the small intestine, diminish cell proliferation and alter the structure and digestive functions.

There are many diseases wherein intestinal structure and functions are altered and Parkinson’s disease (PD) and Diabetes mellitus (DM) are few among them. Diabetes mellitus (DM) which is emerging as a major health problem in the world is a syndrome of disordered metabolism. However,
diabetes is also accompanied by several morphological and functional changes in the small intestinal mucosa and elevated levels of digestive enzymes. Experimental diabetes in rats has been reported to increase the enzymatic activity of many brush border hydrolases including the disaccharidases, stimulate a number of transport systems in the membrane, as well as alter normal histology of intestine. Diabetes mellitus has also been associated with increased intestinal disaccharidase activity and enhanced glucose absorption in humans. Studies have also demonstrated the occurrence of oxidative damage in intestine during experimental diabetes in rats.

Environmental pollutants have now gained the reputation as risk factors for diabetes. Of a wide range of environmental contaminants that pose the danger of health hazard, perhaps, it is OPI that deserve maximum attention for their possible role in acting as predisposing/aggravating factors for risk of diabetes mellitus. Earlier studies have clearly demonstrated that OPI possess the propensity to alter glucose homeostasis and induce hyperglycemia in rats and augment diabetic complications.

Accordingly, the focus of this proposal is to study the potential of selected OPI to modulate intestinal brush border enzyme activities and also to investigate the consequences on intestinal functions. In view of the potency of OPI to interfere with factors associated with pathophysiology of diabetes, the present work has been envisaged to investigate also on the impact of OPI on the intestinal functions in experimentally induced diabetic rats. Thus, the proposal basically addresses three aspects: (a) To assess the propensity of selected 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) To delineate the mechanisms by which the selected OPI modulates the structure and function of small intestine in normal rats.