CONCLUSIONS

1. Single oral dose of MCP equivalent to 1/20 LD$_{50}$ (0.9mg/kg b.w) and 1/10 LD$_{50}$ (1.8mg/kg b.w) and CPF (10 and 20 mg/kg b.w) did not alter the activities of brush border enzymes and redox state markers in any of the intestinal regions. While multiple doses (7d) of MCP induced an increase in the activities of maltase, sucrase and lactase and only maltase activity was increased by multiple doses (7d) of CPF. However, activities of all the three dipeptidases (glycyl-glycine, glycyl-valine and glycyl-leucine) were unaltered with multiple exposures.

2. MCP treated rats exhibited relatively higher increase in the activity of alkaline phosphatase (ALP) in intestine compared to that of CPF. Activity of Na$^+$, K$^+$ ATPase was unaltered with both OPI after 7d, whereas AChE activity was significantly decreased and PON 2 activity was unaltered.

3. Perturbations in redox status were more pronounced in the intestine of rats treated with MCP compared to CPF.

4. In summary, multiple doses (7d) of MCP had more adverse effects on the small intestine compared to CPF. Hence, effect of long-term exposures was carried out with only MCP.

5. In 15d regime, three concentrations of MCP (0.45, 0.9 and 1.8 mg/kg b.w/d i.e. 1/40, 1/20 and 1/10 LD$_{50}$ respectively) were employed. Activities of all the four disaccharidase (maltase, sucrase, lactase and trehalase) were significantly increased in jejunum. Increased activity of ALP and Na$^+$, K$^+$ ATPase was seen in all the three regions at higher doses of MCP.

6. Multiple doses (15d regime) of MCP induced significant decrease in AChE activity, and PON 2 activity was not affected.

7. Enhanced Lipid peroxidation was accompanied with depletion of reduced glutathione levels in the intestine with multiple doses of MCP. Significant reduction in catalase activity in all regions and elevated SOD activity were
evident only in the jejunum with MCP treatment. Further MCP induced significant increase in the activity of GST in duodenum and jejunum.

8. In the long term study (30d regime), MCP induced a significant increase in relative and unit weight of small intestine which was associated with marked increase in intestinal motility measured in terms of intestinal transit.

9. MCP (30d) caused significant reduction in the levels of cholesterol and increased the phospholipid content of intestinal brush border membrane, resulting in decreased cholesterol: phospholipid ratio.

10. All the disaccharidases (maltase, sucrase, lactase and trehalase) activity was significantly increased in all the three regions of the small intestine and maximum increase was evident in jejunum. The activity of glycyl-glycine and glycyl-leucine dipeptidase was also increased in jejunum and ileum.

11. Increased activity of ALP and Na+, K+ ATPase was observed in all the three regions due to exposure to MCP at the higher dose.

12. The inflammatory markers studied (nitric oxide, myeloperoxidase and histamine) showed increased activity clearly suggesting the inflammatory potential of MCP.

13. Mucin content was markedly increased as result of MCP treatment in jejunum and ileum as indicated by increased level of alcian blue binding.

14. Intestinal regions exhibited several histological alterations due to MCP exposure, such as infiltration of inflammatory cells, increased villi length and congestion of villi, goblet cell hypertrophy and hyperplasia.

15. In diabetic model, significant decrease in body weight, increase in relative and unit weight of small intestine was evident in STZ and STZ+MCP groups both in 15 and 30d treatment.

16. Activities of all the tested disaccharidases (maltase, sucrase, lactase and trehalase) were significantly elevated in intestine of rats of all treatment
groups. MCP augmented the disaccharidases activity in STZ rats. Majority of the change was noticeable in jejunum.

17. AChE activity was significantly decreased by MCP (per se treatment) and in diabetic group) in all regions of small intestine. However, AChE activity was increased in intestinal regions of only STZ rats. While MCP (15 d) did not alter PON 2 activity in intestinal regions, the activity was increased in STZ rats. MCP (30d) significantly reduced the PON 2 activity in jejunum and ileum and the extent of decrease was similar to that in STZ rats.

18. Histopathological analysis of intestinal regions revealed that major cellular changes were discernible in jejunum followed by ileum and duodenum. MCP (per se and in diabetic condition) induced changes such as increased villi length, infiltration of inflammatory cells, goblet cell hyperplasia and congestion of villi. MCP treatment among STZ rats resulted in focal areas of necrosis. Alterations were more pronounced in the jejunum (both after 15 and 30d treatment) clearly suggesting its increased susceptibility.

19. Collectively, these findings clearly establish the propensity of OPI to induce biochemical alterations in small intestine of rats after repeated oral doses. The biochemical alterations induced by MCP are likely to affect the functions of the small intestine. Besides affecting the enzymes involved in digestion, MCP treatment also altered intestinal motility.

20. The results of the present study also provide evidence for the potential of MCP to augment dysfunctions in the small intestine of diabetic rats. Further, these results clearly demonstrate that the intestine of diabetic rats are prone to further structural, functional and oxidative damage by MCP which might result in exacerbated intestinal dysfunction.

21. Taken together, these findings in the rat model clearly suggest that MCP residues in foods in the long-term are likely to interfere with the digestive capacity of the small intestine and thus may exert adverse effects on the health of human.