Chapter 6: Summary and Conclusion

SUMMARY OF RESEARCH

- *In silico* studies suggested Metformin and Aspirin as potential IGF-1R inhibitors when compared to standard PQ401. Similarly, Atorvastatin and Fenofibrate were found to be potential inhibitors of FASN as compared to standard Orlistat.
- Our *in vitro* studies, SRB assay and cell cycle confirmed the efficacy of Metformin and Atorvastatin on MCF-7 and HepG2 cell lines.
- Pharmacokinetic data shows that when Metformin (200mg/kg) and Atorvastatin (25mg/kg) was administered by oral gavage and in drinking water, they had a similar AUC. Thus, implying these drugs could be administered in drinking water for chemopreventive study.
- Both male and female C57BL/6 mice fed with HFD developed features of central adiposity, non-alcoholic fatty liver disease, hyperinsulinemia, dyslipidemia, impaired glucose and insulin tolerance at 16th week.
- Metformin and Atorvastatin were found to attenuate DMBA-induced tumor growth dose dependently. Combination thereof was found to have synergistic effect (CI < 1) in attenuating tumor growth rate, incidence and delaying onset of tumor.
- Metformin and Atorvastatin were also found to inhibit DEN-induced liver tumorogenesis dose dependently. Treatment with Met and Ato led to lower incidence of hepatocellular carcinoma and reduced foci of cellular alternations.
- Our data suggests that Met and Ato may act on neoplastic cells by both direct and indirect mechanisms. The direct mechanism was governed through drugs action on IGF-1 and FASN, while the indirect actions were governed through effects on insulin sensitivity, hyperinsulinemia, dyslipidemia and its ultimate effect on IGF-1 and FASN levels.

CONCLUSION

The results of the present study clearly indicated that Metformin and Atorvastatin, which are known to improve dysregulation of energy homeostasis, effectively prevent the development of chemically-induced breast and liver tumorigenesis in metabolically abnormal mice.