CHAPTER 9

SUMMARY AND CONCLUSION

The present study highlighted, the inhibitory potential of MenoAct450 capsule and its standardized therapeutic bioactive compounds on CYP450 and its significant isoforms. The results indicated that, the MenoAct450 and its components shown weak inhibitory potential on CYP3A4 and CYP2D6, when compared to respective positive controls. The change in inhibition was observed with all the DMSO solubilized extract, when compared with the ethanol solubilized extracts. The interaction of individual ingredients and formulation with pooled CYP450's were more with the extract rather than its single components suggesting possible synergistic effects.

From high throughput florometric assay findings, it was observed that, the order of inhibitory potential of the test substances through *in vitro* results were identified as MenoAct450 > TA > GA > EA > BA > BS > SS. MenoAct450, herbal extracts and its bioactive molecules tested in the present study possess very weak interaction with other drug biotransformation, but the observed inhibitory effect on metabolizing enzymes can be highly variable as the constituent content can differ with plant species, source, environment and processing and storage conditions.

Form the *in silico* studies, it was observed that, all the ligands were involved in hydrogen bonding with the binding site residues of CYP450. Overall, molecular docking studies concluded that gallic acid, ellagic acid, β-Sitosterol and Stigmasterol have less glide score and glide energy with both CYP3A4 and CYP2D6 when compared to the respective positive control energy and score. Therefore, the *in silico* prediction was in agreement with the results obtained from the CYP3A4 and CYP2D6 inhibition assays.

No significant changes in pharmacokinetics of oral Simvastatin were demonstrated after medication with MenoAct450 at the recommended dosage regimen for the treatment of menopausal symptoms. It reveals that, there is no clinically relevant CYP3A4 inhibition after MenoAct450 treatment in healthy volunteers. Thus,
pharmacokinetic interaction between MenoAct450 and CYP3A4 substrates is considered clinically insignificant.

Even though results indicated that, MenoAct450 and its bioactive molecules exhibited weak interaction potential in conventional drug biotransformation. Time interval should be considered, based on elimination half-life of therapeutic drugs when administering MenoAct450 capsule. *In vitro, in vivo and in silico* evaluation of herb-CYP450 interactions can be incorporated to find the interaction inducing molecules in the early stages of drug development process.