CHAPTER -7
SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

The present investigation of this work “Studies on Pharmacokinetic Drug Interactions in Hepatic failure model” were evaluated the pharmacokinetic and pharmacodynamic interactions between the drugs in normal, diabetic and hepatic impaired model.

In this work the drug–drug interactions between the anti-diabetic (repaglinide) and antiretroviral drugs (ritonavir, atazanavir and indinavir) were evaluated because these drugs are more likely to cause drug–drug interactions in the clinical practice, moreover antiretroviral drugs causes metabolic syndrome (hyperlipidemia and insulin resistance) on long term usage and also these drugs causes hepatotoxicity in the clinical practice.

The present evaluated combinations-I, II and III, among combination-I (repaglinide plus ritonavir) ritonavir increased the bioavailability of repaglinide might be mainly due to the inhibition of CYP 3A4 mediated metabolism in intestine and hepatic and also inhibition transport by OATP in liver by ritonavir. In combination-II (repaglinide plus atazanavir) atazanavir increased the bioavailability of repaglinide and decreased total body clearance due to inhibition of CYP mediated metabolism, P-glycoprotein effect in the intestine and OATP in intestine and in liver. Combination-III (repaglinide plus indinavir) increased the bioavailability and decreased the total body clearance due to inhibition of CYP 3A4 enzyme in liver and P-glycoprotein effect in the intestine.

Comparatively the combination I did not alter the pharmacokinetics and pharmacodynamics in hepatic failure model as combination II and III, this indicates ritonavir did not potentially inhibit the CYP mediated metabolism and OATP & P-gp transporters, but the combination II and III were potentially inhibited the CYP mediated metabolism and transporters. This study concluded atazanavir and indinavir were the potent inhibitors of repaglinide in rats.
The current has raised the awareness of potential drug-drug interactions between the repaglinide plus ritonavir, repaglinide plus atazanavir and repaglinide plus indinavir in the preclinical models.

**Future recommendations**

- Repaglinide DDIs should be evaluated with new drugs in normal rats.
- Repaglinide DDIs should identify with other anti-retroviral drugs in normal, diabetic and hepatic dysfunction model.
- In hepatic dysfunction there was an alteration in the pharmacokinetics of drug so that we have to evaluate the above combinations in hepatic dysfunction patients and find out the clinical significance of the drug-drug interaction in clinical practice.