9. SUMMARY

- PZQ was successfully incorporated into NS by the solvent evaporation followed by freeze drying method
- The β-CD and cross linker (1:4) exhibited highest solubilization and the PZQ was loaded in NS at weight ratio 1:5 (Drug: NS by weight).
- The morphological evaluation studies showed that the NS are in crystalline stage, which was later confirmed by the FTIR, DSC and XRD studies.
- The in vitro release showed a burst release in both physiological media, indicating rapid dissolution.
- An oral pharmacokinetic study in rats showed that NS changed the pharmacokinetic parameters and resulted in significant improvement (2.12 fold) in the bioavailability of PZQ.
- The optimization of process and formulation variables helped to form SLN of particle size in range of 123-139 nm and encapsulation efficiency of 86%.
- The optimized PZQ SLN were stable during storage conditions. The SLN were also stable in phosphate buffer pH 7.4 however, they were not stable in 0.1NHCl.
- During harsh conditions of autoclaving, the particle size changed but EE was not changed considerably.
- The DSC, XRD studies showed that PZQ is not in crystalline state but in amorphous state within the lipid matrix.
- All the formulation showed initial burst release followed by controlled release in Phosphate buffer pH 6.8 while in 0.1 N HCl all the formulation tend to release high amount of drug(>60%) with in 2 hours.

- The binary SLN were optimized using combination of two lipids (GMS and TP) resulted in particle size near to 100nm (ideal for lymph targeting) and entrapment efficiency > 90%.
- The PZQ BSLN were equally stable as PZQ SLN. The DSC and XRD studies revealed that the PZQ was changed to amorphous state in PZQ BSLN.
- The oral pharmacokinetic study in rats revealed that the SLN improved the bioavailability 3.31fold and 4.1 fold with PZQSLN and PZQ BSLN respectively.
- When administered subcutaneously, the PZQSLN and PZQ BSLN improved the bioavailability 3.3 fold and 3.5 fold respectively.
- On intra-muscular administration of the PZQ SLN and PZQ BSLN, the bioavailability was enhanced approximately 2fold and 2.1 fold respectively; the MRT was enhanced from 4hr to 17hr and 18 hr respectively.
- The intraduodonal administration of SLN in CHM rat model proved the lymphatic uptake of the SLN and resulted in 6fold increase in bioavailability.
- The PZQ SLN increased the permeation of PZQ across hydatid cyst membrane in vitro.
- The intra-cystic concentration across whole cyst membrane was increased well above the minimum effective scolicidal concentration.
- PZQ-SLN significantly enhanced the protoscolicidal activity of the PZQ at low concentrations in comparison to free PZQ (PZQ suspension).
- The PZQ loaded SLN were found very effective against H.Diminuta.
- Moreover, the PZQ SLN were effective against all stages of H.Diminuta.
- However, it requires further *in vivo* evaluations on other diseased models for exploring therapeutic application of PZQ-SLN.

- ❖ The current investigation opens new possibility of successful utilization of binary lipid matrix as a carrier for delivery of water insoluble drug(s).
- ❖ The PZQ-SLN could be a promising vehicle for delivery of PZQ for enhanced bioavailability along with reduction in dosing frequency and better patient compliance.