7 Conclusion

VRL is a second generation semisynthetic vinca alkaloid approved by FDA for the treatment of Metastatic Breast Cancer (MBC) and Non Small Cell Lung Cancer (NSCLC). It is vesicant and also venous irritant in nature and hence causes reactions at injection site (superficial phlebitis accompanied by erythema, pain, and vein discoloration and tenderness along the vein). Moreover, the drug produces neutropenia (main dose-limiting toxicity) peripheral neuropathy, alopecia, constipation, diarrhoea, nausea and vomiting. These all problems necessitate development of suitable carriers which can minimize these size effects without compromising the efficacy. Reducing the effective dose by combining with other molecules or by using a nanotechnology or combining drug molecules and using nanotechnology platform could be a promising strategy. Among the different nanotechnology based approaches, solid lipid nanoparticles have gained immense interest as a drug delivery carrier owing to their unique advantages *viz.* low toxicity, excellent biocompatibility, ability to carry hydrophilic or lipophilic drugs, physical stability, protection of incorporated labile drugs from degradation and controlled or localized release of the active drugs and excellent tolerability. The present study focused on successful development of dual drug loaded nanocarriers for enhancing the anticancer efficacy of vinorelbine as compared to the pristine drug. Dual drug loaded nanocapsules encapsulating VRL and RES were successfully developed and evaluated for *in-vitro* and *in-vivo* efficacy. The developed core shell nanocarriers were found to be capable of encapsulating hydrophilic VRL as well as lipophilic RES to a maximum extent. Firstly, VRL was combined with RES in different ratios and evaluated for synergistic activity. Meanwhile formulations with VRL were developed in order to achieve maximum entrapment and evaluated for anticancer efficacy. Further, the

best formulation was selected for encapsulation of the most synergistic combination and evaluated for *in-vitro* and *in-vivo* anticancer efficacy in 4T1 tumor grafted Balb/c mice model. Moreover, these dd-ACNs showed better efficacy and reduced toxicity compared to free drug and VRL nanoformulations.

Although we have gotten exciting findings in our preliminary studies this concept can be tested further for pharmacokinetics, bio-distribution, venous irritation and hypersensitivity studies utilizing suitable models. In addition, surface functionalization with tumor targeting ligands can also be tested, if this can further improve the efficacy of the developed nanoparticles. Combining with other natural antioxidants can also be tested to further prove if the combination of antioxidants with anticancer drugs can be a promising strategy to improve the efficacy. If the developed formulation strategies continue to show better results, these can be used as platform strategy for the delivery of other anticancer agents in combination with natural antioxidants.