Chapter 7

CONCLUSION

7. Conclusion

In the present study, we have successfully optimized, prepared, and characterized gemcitabine and epigallocatechin-3-gallate-loaded solid lipid nanoparticles. The SLNs were prepared by double emulsification solvent evaporation method. The average particle size and polydispersity index (PDI) of GEM-EGCG SLNs, GEM SLNs, and EGCG SLNs were determined to be 122.8 ± 8.02 nm, 0.1738 ± 0.02; 118.9 ± 12.71 nm, 0.257 ± 0.03; and 117.4 ± 9.37 nm, 0.202 ± 0.05, respectively. The zeta potential of GEM-EGCG SLNs, GEM SLNs, and EGCG SLNs was found to be -35.9 ± 1.6 mV, -33.9 ± 2.1 mV, and -24.0 ± 2.7 mV, respectively. The entrapment efficiency of GEM-EGCG SLNs was calculated to be 95.035 ± 8.6% for GEM and 92.406 ± 11.4% for EGCG. GEM-EGCG SLNs exhibited a sustained drug release profile and followed the Higuchi model of release kinetics. A proportional decrease in the percent cell viability of A549 cells has been noticed with an increase in the concentration of GEM-EGCG SLNs, GEM SLNs, and EGCG SLNs with an IC_{50} value of approximately 10 µg/mL for GEM-EGCG SLNs. The metastatic potential was assessed, and it was observed that SLNs could significantly avert the migration of A549 cells, with 85 % of uncovered scratch wound area after 48 hours of incubation at 5 µg/mL which increased to around 90 % at 50 µg/mL. SLNs were able to be internalized into the nuclei of cells which could be due to their small particle size in the nanometer range. The high apoptotic rate shown by GEM-EGCG SLNs depicts its better anti-tumor activity against A549 cells as compared to other treatment groups along with ROS production which mediated the apoptosis of A549 cells. We found that GEM-EGCG SLNs are stable for the observation period of 3 months with only slight changes in the values of particle size, PDI, zeta potential, and percent entrapment efficiency. Overall, the study postulates the synergistic anti-tumor potential of epigallocatechin-3-gallate co-loaded with gemcitabine in biocompatible solid lipid nanoparticles for use as an anti-cancer therapeutic agent against lung cancer.

Epigallocatechin-3-gallate has synergistically aggravated the anti-cancer efficacy of gemcitabine against lung cancer. GEM-EGCG SLNs had better pharmacokinetics than other treatments, and a high drug targeting index (DTI) value of 17.605 for GEM and 2.118 for EGCG, indicating their effectiveness in targeting the lungs. The DTI value signifies the caliber of the intranasal route of administration to target lungs which outweighs the dose-dependent side effects of chemotherapeutic drugs like GEM and also decreases the dose of these drugs as compared to the intravenous route of administration. The prepared monostearate-based lipidic nanoparticles are safe to use and biocompatible with no pathological lesion encountered in the kidney, liver, and nasal region of the Swiss Albino mice. GEM-EGCG SLNs also showed fewer pathological lesions than other treatments and a lower hemolysis rate of 1.62 ± 0.10 %. These results suggest that GEM-EGCG SLNs could effectively treat lung cancer. The findings of our study pave the way for the exploration of the intranasal route of administration as a means of delivery of anticancer agents against lung cancer.