Abstract

Hepatocellular carcinoma (HCC) is a leading cause of death globally and worst reported diseases for survival as it is poorly responsive to both conventional chemotherapy and mechanism directed chemotherapy. This issue is due to the lack of therapeutic concentration in the tumor tissue coupled with the highly toxic side effects exerted by this compound along with concomitant drug resistance towards tumor heterogenicity. Consequently, the best packaging for the therapy of the HCC involves three components: A potent therapeutic drug, a rationally designed drug delivery vehicles to enrich the target side with optimum concentration of the drug and a surface ligand that can lead to a greater possibility for internalization by tumor cells compared to the normal parenchyma.

The effectiveness of flavonoids (apigenin) would improve using in nanoformulations as per literature. Amphiphilic liposomes protect sensitive flavonoid compounds from denaturing and improve the absorption of the encapsulated molecules. Aptamers are new class of small multifunctional ligands, comprising short single stranded oligonucleotides about 30-80 bases in length with high affinity and specificity for their targets. They are developed from RNA or ssDNA libraries via an experimental directed process referred to as systematics evaluation of ligands by exponential enrichment (SELEX).

This thesis provides an insight into the development of tumour-sensing Phosphorothioated and amino-modified aptamer (AS1411)-conjugated stealth nanoliposomes, encapsulating with apigenin for precise and significant biodistribution of apigenin into the target tumour to exploit maximum bio-therapeutic assistances. The stable aptamer functionalized PEGylated nanoliposomes (Apt-NLCs) had an average vesicle size of 100–150 nm, a smooth surface, and an intact lamellarity, as ensured by advanced microscopic studies. This study has specified in vitro process of optimum drug (apigenin) extrusion into the cancer cells by nucleolin receptor-mediated cellular internalization when delivered through modified AS1411 functionalized

PEGylated nanoliposomes and ensured irreversible DNA damage in HCC. Significant improvement in cancer cell apoptosis in animal models, due to reduced clearance and higher intratumor drug accumulation along with almost nominal toxic effect in liver, strongly supports the therapeutic potential of aptamer-conjugated PEGylated nanoliposomes compared to the nonconjugated formulations in HCC. The study has established a robust superiority of modified AS1411 functionalized PEGylated nanoliposomes as an alternative drug delivery approach with momentous reduction of HCC tumour incidences.