ABSTRACT

Tamoxifen citrate (TMC) stops and prevents cell multiplication and development of breast cancer. Novel triaryl (Z)-olefin (TZO) as Tamoxifen analogue was synthesized due to development of resistance, limited activity and toxicity of TMC. TZO is more effective than TMC by two folds. The aim of this thesis was to describe an in-situ pH responsive niosomes as a carrier for localized and sustained delivery of TZO. TZO and TMC loaded niosomes were developed by Design-Expert software using different non-ionic surfactants (NIS) [Sorbitan monostearate (Span 60), Sorbitan monooleate (Span 80) and Polysorbate 80 (Tween 20)] and cholesterol in different molar ratios (1:1, 1:2 and 1:3). The prepared formulae were characterized for entrapment efficiency (EE), in-vitro release studies for 8 hours (h) and the vesicle size. TZO and TMC loaded niosomes formulae prepared using equi-molar ratio of Span 60 and cholesterol were selected as optimum formulae where they exhibited a distinct nano-spherical shape with EE% up to 88.90% and 91.18% respectively and slow drug release pattern. Then, the optimized formulae were incorporated into chitosan and Glyceryl monooleate (C/GMO) solutions as a localized in-situ pH sensitive hydrogel delivery system. Design-Expert software was used to determine the effect of C/GMO on viscosity and in vitro release studies for 8 h. The results displayed that the release rate was significantly antagonistic with both of C/GMO concentrations while viscosity was significantly synergistic with both of them. The optimum formulae were selected and capped with gold as an ideal candidate for computed tomography to evaluate the efficacy and tissue distribution of TZO compared with TMC using Ehrlich carcinoma mice

model. The optimum formula showed localized TZO in the tumour and consequently significant anti-tumour efficacy. Based on these results, the novel in situ pH sensitive TZO loaded niosomes could be a promising formula for efficient treatment of breast cancer**.**

Thus the work in this thesis was divided into three chapters:

Chapter I: Formulation and *in vitro* evaluation of Tamoxifen Citrate and Tamoxifen analogue loaded Niosomes

Chapter II: Formulation and *in vitro* evaluation of in situ pH sensitive hydrogel formulae.

Chapter III: *In vivo* evaluation of an optimized in situ pH sensitive Tamoxifen Citrate and Tamoxifen analogue loaded niosomes hydrogels.