

Optimization of nanoemulsion containing gemcitabine and evaluation of its cytotoxicity towards human fetal lung fibroblast (MRC5) and human lung carcinoma (A549) cells

ABSTRACT

Background: Gemcitabine (GEM) is a chemotherapeutic agent, which is known to battle cancer but challenging due to its hydrophilic nature. Nanoemulsion is water-in-oil (W/O) nanoemulsion shows potential as a carrier system in delivering gemcitabine to the cancer cell.

Methods: The behaviour of GEM in MCT/surfactants/NaCl systems was studied in the ternary system at different ratios of Tween 80 and Span 80. The system with surfactant ratio 3:7 of Tween 80 and Span 80 was chosen for further study on the preparation of nanoemulsion formulation due to the highest isotropic region. Based on the selected ternary phase diagram, a composition of F1 was chosen and used for optimization by using the D-optimal mixture design. The interaction variables between medium chain triglyceride (MCT), surfactant mixture Tween 80: Span 80 (ratio 3:7), 0.9 % sodium chloride solution and gemcitabine were evaluated towards particle size as a response.

Results: The results showed that NaCl solution and GEM gave more effects on particle size, polydispersity index and zeta potential of 141.57 ± 0.05 nm, 0.168 and -37.10 mV, respectively. The optimized nanoemulsion showed good stability (no phase separation) against centrifugation test and storage at three different temperatures. The in vitro release of gemcitabine at different pH buffer solution was evaluated. The results showed the release of GEM in buffer pH 6.5 (45.19%) was higher than GEM in buffer pH 7.4 (13.62%). The cytotoxicity study showed that the optimized nanoemulsion containing GEM induced cytotoxicity towards A549 cell and at the same time reduced cytotoxicity towards MRC5 when compared to the control (GEM solution).

Keyword: Gemcitabine; Water-in-oil nanoemulsion; Hydrophilic drug; Lung cancer; Doptimal mixture design