Improvement of physicochemical properties of nanocolloidal carrier loaded with low water solubility drug for parenteral cancer treatment by response surface methodology

ABSTRACT

Nanoemulsions have been used as a drug carrier system, particularly for poorly water-soluble drugs. Sorafenib is a poorly soluble drug and also there is no parenteral treatment. The aim of this study is the development of nanoemulsions for intravenous administration of Sorafenib. The formulations were prepared by high energy emulsification method and optimized by using Response Surface Methodology (RSM). Here, the effect of independent composition variables of lecithin (1.16–2.84%, w/w), Medium-Chain Triglycerides (2.32–5.68%, w/ w) and polysorbate 80 (0.58–1.42%, w/w) amounts on the properties of Sorafenib-loaded nanoemulsion was investigated. The three responses variables were particle size, zeta potential, and polydispersity index. Optimization of the conditions according to the three dependent variables was performed for the preparation of the Sorafenib-loaded nanoemulsions with the minimum value of particle size, suitable rage of zeta potential, and polydispersity index. A formulation containing 0.05% of Sorafenib kept its properties in a satisfactory range over the evaluated period. The composition with 3% Medium-Chain Triglycerides, 2.5% lecithin and 1.22% polysorbate 80 exhibited the smallest particle size and polydispersity index (43.17 nm and 0.22, respectively) with the zeta potential of −38.8 mV was the optimized composition. The fabricated nanoemulsion was characterized by the transmission electron microscope (TEM), viscosity, and stability assessment study. Also, the cytotoxicity result showed that the optimum formulations had no significant effect on a normal cell in a low concentration of the drug but could eliminate the cancer cells. The dose-dependent toxicity made it a suitable candidate for parenteral applications in the treatment of breast cancer. Furthermore, the optimized formulation indicated good storage stability for 3 months at different temperatures (4 ± 2 °C, 25 ± 2 °C and 45 ± 2 °C

Keyword: Nanoemulsion; Parenteral delivery; Anti-cancer; Sorafenib; Response surface methodology