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Abstract

Co-encapsulation of doxorubicin and vorinostat in polymeric nanoparticles for the breast cancer therapy †

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Abstract: Recent data revealed that the combined administration of histone deacetylase inhibitors such as vorinostat (suberoylanilide hydroxamic acid, SAHA), with genotoxic agents, such as doxorubicin (DOX), enhances the antitumoral effects of both drugs against solid tumors. Herein we designed nanoparticles based on copolymer of lactic and glycolic acids (PLGA) simultaneously loaded with DOX and SAHA to provide synergy against tumor cells. We obtained the nanoparticles via double emulsion solvent evaporation technique with dichloromethane as the organic solvent and polyvinyl alcohol (PVA) as the emulsion stabilizer. To optimize the nanoformulation, a 12-run, three-factor, three-level Box-Behnken design was used. We investigated the influence of PLGA amount (X1), dichloromethane volume (X2), and PVA concentration (X3) on the nanoparticle size (Y1) and SAHA drug loading (Y2). Next, we optimize the factors via desirability function. After optimization the calculated values for nanoparticle size was 203 nm and for SAHA drug loading was 0.5 %. Experimental data revealed that optimized conditions provided the nanoparticles with a size of 207±8 nm and SAHA drug loading of 0.9 %, which is close to calculated data. Besides these parameters nanoparticles had ζ-potential of -18.0±4.6 mV and DOX drug loading of 2.1 %. The optimization approach used in this work allowed the determination of the factors required to produce nanoparticles with minimum size and maximum drug loading of SAHA. Furthermore, the calculated responses were close to the experimental data. Thus, the obtained dual-drug loaded PLGA nanoparticles had suitable physical properties for promising further studies in vitro and in vivo.

Keywords: vorinostat; doxorubicin; PLGA; polymer particles, breast cancer, Box-Behnken design; co-encapsulation

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