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Nanoformulations for Hsp90 inhibitors for cancer therapy

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Heat shock protein (Hsp) 90 plays an important role in maintaining protein homeostasis and helps in cancer proliferation. Molecules targeting Hsp90 in multiple cancers have entered advanced clinical trials. However, Hsp90 targeted cancer therapy faces a major problem of the aqueous dispensability of drugs due to their hydrophobic nature. Nanoformulation using soft polymers has played an important role in the aqueous delivery of hydrophobic anticancer drugs. Hence, to address the formulation issue of hydrophobic-Hsp90 targeted drugs, we have developed Hsp90 inhibitors loaded polymeric nanoformulations, which can be dispensed using aqueous phase (devoid of organic solvents). We have developed 17AAG (first generation Hsp90 inhibitor) and Fe_3O_4 loaded PLGA magnetic nanoparticles (MNPs). We had developed two types of formulations (1:1:10 and 1:1:20) by relatively varying the concentration of PLGA polymer. Our study showed that ratio of 1:1:10 for (17AAG, Fe_3O_4 and PLGA) provided relatively better physicochemical and pharmacological response. The size of drug loaded polymeric MNPs from 1:1:10 nanoformulation were found to be 204 nm (confirmed with SEM and TEM images). These NPs provided dual mode of Pancreatic Cancer (MiaPaCa-2) cells destruction under in vitro conditions; rendered by magnetic hyperthermia (provide by Fe3O4) and Hsp90 inhibition (rendered by 17AAG). We have also developed novel albumin conjugated Hsp90 inhibitor loaded nanoparticles. We used standard desolvation method for the synthesis of drug conjugated albumin nanoparticles. Our studies showed that nab-Hsp90 inhibitor nanomedicine was found to have average particle size of around 222 nm (confirmed with high-resolution SEM and TEM images). Our study shows that the synthesized drug loaded albumin nanoparticles were found to be effective under in vitro condition against both pancreatic (MiaPaCa-2) and breast cancer (MCF7) cell lines. Our studies indicate that our nanomedicine platform, which consists of both synthetic and natural (protein based) polymers that can play a significant role the delivery of Hsp90 targeted anticancer drugs for next-generation anticancer therapy.

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