At the crossroad of drug discovery and delivery- PARP inhibitors and hollow metallic nanoparticles in cancer therapeutics

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Development of PARP inhibitors as cytotoxic leads in cancer therapeutics

Poly ADP-ribose polymerase-1 (PARP-1) is a nuclear enzyme essential to the repair of single strand DNA breaks via the base excision repair/single strand break repair pathway. Our lab has synthesized a series of heterocyclic compounds as potential PARP-1 inhibitors. Among these, quinazolinone scaffold based analogues have shown good activity. A series of twelve 2-styryl quinazolin-4(3H)-one analogues were synthesized by condensation of 2-methyl quinazolin-4(3H)-one with appropriate aromatic aldehydes. This scaffold was further used to synthesize a series of hybrids with pyrimidine analogues They were screened for cytotoxicity against MCF-7 cells using sulforhodamine B assay. The percentage yield of synthesized compounds was found to be in the range of 60 to 90%. The GI_{50} of 4-nitrophenyl ethan-1-ene quinazolin-4-(3H)-one was found to be 8.1μg/mL comparable to standard Adriamycin. Flow cytometry study for the 4-nitrophenyl ethan-1-ene quinazolin-4-(3H)-one and 2-nitrophenyl ethan-1-ene quinazolin-4-(3H)-one indicated that the cells in early apoptosis were ~20% indicating caspase mediated death. Few of these along with the hybrid series were found to be potent with good PARP-1 inhibitory activity.

Design and synthesis of functionalized hollow metallic nanoparticles in cancer therapeutics

Metallic nanostructures with hollow interiors are excellent agents for biomedical applications due to their Surface Plasmon Resonance (SPR) in Vis-NIR range. We report for the first time, an extensive study on the effect of (1) the addition sequence of stabilizer, (2) type of stabilizer, (3) the concentration of reducing agent ($NaBH_4$) and (4) the reaction temperature on the SPR characteristic of glutathione-capped hollow silver nanoparticles (GSH-HAgNPs) using the sacrificial Ag_2O template. The photoablation of functionalized metallic nanoparticles (SPR at 531 nm) using a 532 nm Nd:YAG 300 mW continuous wave (CW) laser led to a 5–6^oC elevation in temperature above physiological temperature within 15 minutes suggesting the use of GSH as hyperthermia-inducing agent. This study provides an evidence of the potential application of functionalized hollow metallic nanoparticles in biomedicine, especially as drug delivery cargoes in cancer therapeutics.