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PEGylated-thymoquinone-nanoparticle mediated retardation of breast cancer cell migration by deregulation of cytoskeletal actin polymerization through miR-34a

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Thymoquinone (TQ), a major active constituent of black seeds of *Nigella sativa*, has potential medical applications including spectrum of therapeutic properties against different cancers. However, little is known about their effect on breast cancer cell migration, which is the cause of over 90% of deaths worldwide. Herein, we have synthesized TQ-encapsulated nanoparticles using biodegradable, hydrophilic polymers like polyvinylpyrrolidone (PVP) and polyethyleneglycol (PEG) to overcome TQ's poor aqueous solubility, thermal and light sensitivity as well as consequently, minimal systemic bioavailability which can greatly improve the cancer treatment efficiency. Synthesized TQ-NPs were physico-chemically characterized by UV-Vis spectroscopy, DLS, zeta potential analyzer, FT-IR spectroscopy, XRD, FESEM, TEM, H1-NMR and TGA. Sizes of synthesized TQ-Nps were found to be below 50 nm and they were mostly spherical in shape with smooth surface texture. In the present investigation, we provide direct evidence that TQ-Nps showed more efficiency in killing cancer cells (MCF-7, HBL-100) as well as proved to be less toxic to normal cells at a significantly lower dose than TQ. Interestingly, evaluation of the anti-migratory effect of the TQ-Nps, revealed that PEG_{4000}-TQ-Nps showed much potent anti-migratory properties than the other types. Further studies indicated that PEG_{4000}-TQ-Nps could significantly increase the expression of miR-34a through p53. Moreover, NPs mediated miR-34a up-regulation directly down-regulated Rac1 expression followed by actin depolymerisation thereby disrupting the actin cytoskeleton which leads to significant reduction in the lamellipodia and filopodia formation on cell surfaces thus retarding cell migration. Considering the biodegradability, non-toxicity and effectivity of PEG_{4000}-TQ-Nps against cancer cell migration, TQ-Nps may provide new insights into specific therapeutic approach for cancer treatment.

Biography

Arghya Adhikary has completed his PhD from Bose Institute and Postdoctoral studies from same institute. He is now DST INSPIRE Faculty, Assistant Professor at Centre for Research in Nanoscience and Nanotechnology, University of Calcutta. He has published more than 25 papers in reputed journals related to Cancer cell signaling, majorly on breast cancers and has been working on Nano-Bio interphase for the last two years. His research area is focused on the synthesis of biocompatible nanoparticles of different plant polyphenols to be used for cancer nanotherapeutics.

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