

Defence Seminar

Seminar Title	: Elucidating the Berberine-Induced Epigenetic Regulation of Nrf2 Signaling Axis and Its Targeted Delivery via Folate-Functionalized Bovine Serum Albumin Nanocarriers against Glioblastoma
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Venue	: Mathematics Seminar room
Date and Time	: 09 Apr 2025 (03.30PM)
Abstract	: Glioblastoma multiforme (GBM) represents one of the most aggressive and lethal brain cancers, characterized by rapid proliferation, invasive growth, and poor prognosis. Natural products with multiple pharmacological properties have surfaced as promising agents against various cancers. Berberine, a isoquinoline alkaloid, has exhibited considerable anti-cancer activity. Our study demonstrates that berberine's mode of action involves multiple pathways, including triggering apoptosis, inhibiting cell migration, inducing cell cycle arrest, and causing DNA damage, which is primarily mediated through mitochondrial dysfunction facilitated by ROS generation. Further, it was found that berberine downregulates the Nrf2 antioxidant signaling pathway in GBM cells. The mechanistic analysis reveals that berberine decreases the expression of KDM6B, resulting in an increased occupancy of H3K27me3 at the Nrf2 promoter, suppressing downstream signaling of the Nrf2 pathway. Further, to improve the efficiency of berberine, a novel drug delivery system employing BSA nanoparticles was developed to encapsulate berberine thereby improving its stability and bioavailability. The FESEM and TEM analysis of these BER-BSA NPs revealed a spherical morphology. Further, in vitro cell culture evaluations in LN229 cells indicated that BER-BSA NPs produced more significant cytotoxic effects than free berberine, suggesting that the nanoparticle formulation enhances the therapeutic potency of berberine. Additionally, enhanced inhibition of cell migration, increased apoptosis, nuclear condensation, reduction of mitochondrial membrane potential, and elevated ROS production were observed. To enhance the GBM-specific targeting capability of the delivery system, folic acid was conjugated to BSA nanoparticles, taking advantage of the overexpression of folate receptors in glioblastoma cells. The resulting FA-BER-BSA NPs maintained a spherical shape, and the successful conjugation of folic acid to BER-BSA NPs was validated through FTIR and UV- Vis spectroscopy. The in vitro evaluations on LN229 cells showed that these FA-BER-BSA NPs possessed superior cytotoxic effects compared to their non-targeted ones. The enhanced cytotoxicity was further corroborated with enhanced inhibition of cell migration, nuclear condensation, ROS generation, mitochondrial membrane damage, apoptosis induction, and cell cycle arrest. Subsequently, enhanced cellular uptake of FA-BER-BSA NPs was evidenced by fluorescence microscopy and flow cytometry analysis conducted with LN229 monolayers and tumor spheroids. The study demonstrates the efficacy and safety of FA-BER-BSA nanoparticles as a targeted drug delivery system, combining folic acid's precision targeting with berberine's anti-cancer activity, offering a promising approach for glioblastoma treatment in precision oncology. KEYWORDS: Berberine, Glioblastoma, ROS Production, Mitochondria Membrane disruption, Epigenetic regulation, BSA nanoparticles, Folic acid Targeting.