National Institute of Technology Rourkela

Synopsis Seminar

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| 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 |
| Speaker | : Sayantan Ghosh ( Rollno : 519ls1009) |
| Supervisor | : Prof.(Ms.) Bismita Nayak |
| Venue | : LS Seminar room |
| Date and Time | : 25 Nov 2024 (5.00 PM) |
| Abstract | : **Abstract** |


Glioblastoma multiforme (GBM) represents one of the most aggressive and lethal brain cancers, characterized by rapid proliferation, invasive growth, and poor prognosis. Standard regimens mandate surgical resection, followed by radiotherapy with conventional chemotherapy, usually temozolomide. Natural products with multiple pharmacological properties have surfaced as promising agents against various cancers. Berberine is a naturally occurring isoquinoline alkaloid, which has received significant attention for its wonderful anticancer activities, mainly induction of apoptosis, inhibition of migration, cell-cycle arrest, and DNA damage in GBM cells through mitochondria dysfunction mediated by reactive oxygen species (ROS). We found the Nrf2 antioxidant pathway is suppressed by berberine, which is an important pathway in GBM chemoresistance. In this study, berberine downregulate KDM6B, leading to an increase in H3K27me3 levels on the Nrf2 promoter, thereby suppressing Nrf2 expression, hence inhibiting the downstream signaling pathways. In spite of the attractive potential of berberine in its therapeutic application, its clinical translation has been delayed by unsatisfactory solubility, rapid metabolism, and limited bioavailability. To address these challenges, we developed a new nanocarrier system using bovine serum albumin (BSA) nanoparticles encapsulated with berberine to increase its stability and delivery. We confirmed the particles to be spherical with an average diameter of ~90 nm after the SEM and TEM observations. XRD, FTIR, UV-Vis, and DSC analyses revealed tha encapsulation of berberine inside BSA nanoparticles. Toxicological evaluation in vitro in LN229 cells revealed that, compared to BER, BER-BSA NPs showed higher cytotoxicity with augmentation of migration inhibition, apoptosis, nuclear condensation, mitochondrial membrane potential loss, and ROS production. Furthermore, we wanted those nanoparticles to target glioblastoma specifically therefore, we conjugated folic acid to BSA nanoparticles because of the overexpression of folate receptors in glioblastoma cells. The resulting folic acid-functionalized berberine-loaded BSA nanoparticles (FA-BER-BSA NPs) were spherical with an optimized particle size of 120-140 nm, as confirmed by SEM and TEM. The results found *in vitro* in the glioblastoma LN229 cell line show that FA-BER-BSA NPs, in comparison with nonfunctionalized counterparts, exhibited enhanced cytotoxicity, migration inhibition, and apoptosis induction this is likely due to increased cellular uptake in monolayer cells and 3D tumor spheroids via folate receptor-mediated endocytosis. These findings support the potential of FA-BER-BSA NPs as a targeted therapeutic approach, presenting a viable strategy for overcoming GBM's inherent resistance and enhancing the efficacy of berberine in glioblastoma treatment.



**KEYWORDS:** Berberine, Glioblastoma, ROS Production, Mitochondria Nembrane disruption, Epigenetic regulation, BSA nanoparticles, Folic acid Targeting.