National Institute of Technology Rourkela

Synopsis Seminar

Seminar Title	: Investigating the anticancer potential of Shikonin by targeting PLK1 and enhancing therapeutic efficacy through micellar encapsulation in oral squamous cell carcinoma
Speaker	: Stuti Biswal (Rollno : 519ls2019)
Supervisor	: Prof. Bijesh Kumar Biswal
Venue	: Life Science Seminar Hall
Date and Time	: 13 Jan 2025 (11.00 AM)
Abstract	: Natural Natural bioactive alkaloid phytocompound shikonin is found in the *Lithospermum erythrorhizon* plant&rsquos root and exhibits excellent pharmacological properties including anticancer activity. This study explores the mechanistic role of shikonin (Shk) in the proliferation and migration of oral squamous cell carcinoma (OSCC) cells. Shikonin suppresses the viability of SCC9 and H357 OSCC cells in a time and concentration-dependent manner. It promotes the generation of intracellular reactive oxygen species which then leads to the depletion of mitochondrial membrane potential (MMP). Further, this causes DNA damage and cell cycle arrest in the G2/M and S-G2/M phases in SCC9 and H357 cell lines respectively. The interaction of DNA and Shk was confirmed by docking and CD spectroscopy and EtBr displacement assay. Shk also induces apoptosis in OSCC cells by enhancing the expression of Bax and Caspase 3. It also suppresses colony formation and tumorigenicity in a dose-dependent manner. The molecular mechanism behind the anticancer activity of shikonin was analyzed using bioinformatics studies. The molecular docking and dynamic simulation studies revealed that shikonin makes stable binding with polo-like kinase 1 (PLK1), a key target highly upregulated in OSCC and possibly inhibits its function. It was observed that the expression level of PLK1 mRNA was decreased compared to the control upon shikonin treatment. Interestingly, the knockdown of PLK1 reduces the proliferation and viability of OSCC cells while promoting apoptosis and DNA damage, similar to the shikonin treatment. Instead of having excellent anticancer properties the clinical use of shikonin is still limited because of its poor bioavailability, solubility, and stability. To overcome this problem, polymeric micelles are used as a drug delivery vehicle. These micelles are smaller in size which helps easy penetration in cancer cells with increased permeability and retention effect. Here mPEG-SA micelles are used for shikonin encapsulation. The formation of blank and drug-loaded micelles is characterized by ^{1}HNMR, FTIR, CMC, drug-loading, and encapsulation efficiency, DLS, DSC, TEM, and drug release time. It was confirmed that the micelles were properly formed and the drug was successfully encapsulated. The blank micelles show no cytotoxicity to the OSCC cells. The shikonin-loaded micelles show better and prolonged toxicity compared to only shikonin treatment causing cell death of OSCC cells. Hence, it can be concluded that shikonin-loaded mPEG-SA micelles can be used as a therapeutic agent for effective delivery of this phytocompound in OSCC cells, which can give prolonged and better anticancer effects.