Nebulization based Inhalation Nanomedicine for Lung Cancer Treatments

Rahul Tiwari
The University of Texas Rio Grande Valley, rahul.tiwari@utrgv.edu

Meghana Kolli
The University of Texas Rio Grande Valley, meghana.kolli01@utrgv.edu

Neeraj Chauhan
The University of Texas Rio Grande Valley, neeraj.chauhan@utrgv.edu

Eswara Naga Hanuma
The University of Texas Rio Grande Valley, eswaranagahanumakumar.ghali@utrgv.edu

Vivek Kashyap
The University of Texas Rio Grande Valley, vivek.kashyap@utrgv.edu

See next page for additional authors

Presenter Information (List ALL Authors)
Rahul Tiwari, Meghana Kolli, Neeraj Chauhan, Eswara Naga Hanuma, Vivek Kashyap, Subhash Chauhan, and Murali Yallapu

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Tiwari R[1,2], Kolli M[1,2,] Chauhan N[1,2,] GENH Kumar[1,2,] Kashyap VK, Chauhan SC[1,2,] Yallapu MM[1,2*]

[1]Department of Immunology and Microbiology, Medicine and Oncology Service Unit, School of Medicine, University of Texas Rio Grande Valley, McAllen, TX, 78504, USA

[2]South Texas Center of Excellence in Cancer Research, Medicine and Oncology Service Unit, School of Medicine, University of Texas Rio Grande Valley, McAllen, TX 78504, USA

Background:
Lung cancer is reported to have a high incidence rate and first leading cause of cancer-related morbidity and mortality across the world including in the United States. Noninvasive nebulized inhalation is a promising delivery strategy for lung, which can enhance the targeting efficiency and detention time interval of nanoparticles in the lung tissue, thus elevating the therapeutic index of therapeutic agent(s) at lower dosages. The aim of this study is to develop inhalable nanoparticles (INPs) for effective delivery of therapeutic agents in lung cancer cell lines and *ex vivo* models.

Methods:
The inhalation nanoparticles (INPs) were prepared by solvent evaporation and self-assembly approach. The INPs formulations were characterized by particle size, chemical composition, and drug loading efficiency using various analytical methods including FT-IR, DSC, SEM, and DSC/TGA. Cellular uptake of INPs was evaluated in 2D and 3D models of lung cancer cell lines (A549 and NCI-H1299) using fluorescence microscopy and flow cytometry analysis. Additionally, the therapeutic evaluation of gambogic acid and gemcitabine encapsulated INPs was performed by basic in vitro biological assays using proliferation (CCK-8), mucoadhesion Boyden chamber, and apoptosis assays using lung cancer (A549 and NCI-H1299) monolayers, spheroids, and xenograft tumors.

Results: The developed INPs exhibited an average size of ~110 nm in dynamic light scattering measurements. INPs formulation showed a remarkable mucoadhesion and mucopenetration potential in-vitro model(s). Cellular uptake studies demonstrated that INPs formulation facilitates an effective endosomal release into the cytosol. The in vitro study confirms that INPs release the drugs in a sustained manner. Additionally, the INPs formulation showed superior in vitro anti-cancer activity in lung cancer cell lines, spheroids and xenograft tumor.

Conclusions: Altogether this study confirms that INPs formulation demonstrates an improved therapeutic benefit over free drug against lung cancer cell lines, spheroids and xenograft tumor. This study could lead as an innovative therapeutic modality for the treatment of lung cancer.