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Dual loaded actively targeted liposomes for anti-resistance treatment of melanoma**Harshita Mishra¹, Sushama Talegaonkar^{1,2}, Zeenat Iqbal¹ and Manu Jaggi³**¹Jamia Hamdard University, India²Delhi Pharmaceutical Sciences and Research University, India³Dabur Research Foundation, India

Melanoma is one of the deadliest cancers with very low response and survival rates. Main reason of poor outcomes of therapy is the inherent resistance of melanoma cells. Survivin is a protein which is overexpressed by melanoma cells and is known to impart resistance to them against apoptosis which is supposed to be induced by chemotherapy. Eugenol has been reported to inhibit survivin in breast cancer cells. Thus, in order to fight resistant melanoma in a more efficient manner, we formulated hyaluronic acid (HA) coated liposomes loaded with eugenol along with dacarbazine which is the gold standard chemotherapeutic agent used for melanoma treatment. After synthesizing the liposomes using solvent injection method, QbD was applied to optimize and obtain a final formulation with desired quality attributes. The optimized formulation was then subjected to performance analysis in cell lines and animals. Coated-Dacarbazine Eugenol Liposomes were found to possess almost 9 folds more cytotoxicity than dacarbazine solution against melanoma cell lines (at dacarbazine concentration of 0.5 µg/ml). The number of late apoptotic cells was also found to be much higher in formulation treated cells in comparison to dacarbazine solution treated cells. Migration assay and proliferation study also indicated towards considerably greater inhibition of cell

migration and proliferation by Coated-Dacarbazine Eugenol Liposomes, signifying its potential against metastasis. Results of pharmacodynamic study on melanoma bearing C57BL/6 mice revealed that our formulation could significantly delay the tumor growth in comparison to dacarbazine solution; and biodistribution study confirmed the long circulating nature of the formulation. Thus, the results of this study indicate towards better possibilities of melanoma treatment if the treatment is focused on specific resistance mechanism of this deadly cancer.

Speaker Biography

Harshita Mishra is about to finish her doctorate in Pharmaceutics from Jamia Hamdard University, India. She has 14 international publications and around 300 citations. She has also written 5 book chapters in books edited by Elsevier, Stanford etc. Her educational background includes Bachelor of Pharmacy, Master of Pharmacy and Post Graduate Diploma in Intellectual Property Rights. She is a two times qualifier of GPAT which is an all India level aptitude and evaluation exam. She has twice received Elsevier's 'Top 25 Hottest Articles' award for her paper on metal nanoparticles. She has presented papers in 7 International and National Conferences and won awards in 3 of them. Her areas of interest include Nanotechnology and Cancer treatment.

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