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To whom so ever it may concern

I confirm that work entitled **"NANO LIPID CARRIER BASED TARGETED DUAL DRUG DELIVEY OF 5-FLUOROURACIL AND CANNABIDIOL FOR TREATMENT OF SKIN CANCER"** was carried out by **Mr. Nazeer Hasan** under my supervision during his studies he worked on non-melanoma skin cancer as it is one of most common malignancies reported with high number of morbidities, demanding an advanced treatment option with superior chemotherapeutic effects. Due to high degree of drug resistance, conventional therapy fails to meet the desired therapeutic efficacy. To break the bottleneck, nanoparticles have been used as next generation vehicles that facilitate the efficient interaction with the cancer cells. Initially, he developed a simple and robust HPLC method for simultaneous estimation of 5-FU and CBD at its single wavelength (237 nm) and validated the same. The method could effectively quantify the nanogram levels of both analytes simultaneously in plasma spiked samples and in various nanoformulations. Then, he developed combined therapy of 5-fluorouracil (5-FU) and cannabidiol (CBD)-loaded nanostructured lipid carrier gel (FU-CBD-NLCs gel). The NLCs were optimized using central composite design that showed an average particle size of 206 nm and a zeta potential of -34 mV. In addition, in vitro and ex vivo drug permeations studies demonstrated the effective delivery of both drugs in the skin layers via lipid structured nanocarriers. Also, the prepared FU-CBD-NLCs showed promising effect in-vitro cell studies including MTT assays, wound healing and cell cycle as compared to the conventional formulation. Moreover, dermatokinetic studies shows there was superior deposition of drugs at epidermal and the dermal layer when treated with FU-CBD-NLCs. Furthermore, confocal microscopy study results showed excellent uptake and deposition at epidermal and the dermal layer. Irritation studies performed by IR camera and HET cam shows FU-CBD NLCs was much more tolerated and less irritant compared to conventional treatment. Gamma scintigraphy evaluation shows the skin retention behaviour of the formulation. Later, in-Ovo tumor remission studies were performed, and it was found that prepared FU-CBD NLCs was able to reduce tumor volume significantly compared to conventional formulation. Thus, obtained results disclosed that permeation and disposition of 5-FU and CBD into different layers of the skin FU-CBD NLCs gel could be more potential carrier than conventional gel. At last, prepared formulation showed greater tumor remission, better survival rate, reduction in tumor number, area, and volume with improved biochemical profile. Thus, prepared gel could serve as a promising formulation approach for the skin cancer treatment.

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