Ramesh Chandra, Madridge J Cancer Stud Res. 2019
http://dx.doi.org/10.18689/2640-5180.a4.005

Preclinical to Clinical Milestones in Success of Noscapinoids: Opportunities and Challenges

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Over the past decade, the cancer incidence rate was stable in women and declined by approximately 2% annually in men, while the cancer death rate declined by about 1.5% annually in both men and women. Doctors and scientists are always looking for better treatment ways to cure people having cancer. Hence, they create and study new anticancer drugs. Moreover, they also look for new pathways to deliver drugs in tumor tissues that are already available. Drug discovery to drug delivery is a long development and approval process. During this process, researchers make sure that the drug should be safe for patients to take and effectively treats cancer. This process often takes many years and significant resources.

The armamentrum of chemotherapy is generally used to target specific cellular mechanisms in the malignant tissues. Chemotherapeutic agents usually disrupt the vital parts of the cancer cell that consequently prevent cell division. Treatment of cancer requires combination of both radiation and chemotherapy, respectively.

Our group had discovered the anticancer potential of Noscapine, a phthalideisoquinoline alkaloid obtained from the plant "*Papaver somniferum*". Later, several potent analogues of noscapine such as 9-bromonoscapine, chloronoscapine, 9-amino-noscapine and reduced bromo-noscapine were synthesized and reported by our group. These potent analogues were collectively termed as "Noscapinoids".

Recently, several preclinical analyses of noscapinoids against human or mouse tumor cells such as human cervical cancer (HeLa) cells, human non-small cell lung cancer (A549) cells and mouse melanoma cancer (B16F1) cells substantiated that noscapinoids exert potent anticancer activity against cancer cells and even tailored analogues are also toxic to resistant cancer cells. Apart from cancer, noscapine also exhibited potential in the treatment of experimental polycystic ovary syndrome and stroke. Hence, owing to encouraging preclinical consequences, noscapine is currently undergoing Phase I clinical trial against multiple myeloma.

Likewise other anticancer drugs, noscapinoids also exhibit poor physicochemical and biopharmaceutical chattels. The oral absolute bioavailability of noscapine is reported in the range of 40-50% that may be credited to low aqueous solubility. Nevertheless, these properties created both challenges as well as opportunities for formulation scientists to develop a clinically viable formulation for the treatment of cancer.

Thanks to era of nanoscaled drug delivery systems that are providing opportunities to young scientists for developing novel clinically viable formulations to fight cancer. Abraxane (Human serum albumin-paclitaxel conjugate) is one of the commercially successful formulations. Hence, our group reported the cyclodextrin complexes, nanoparticles, effervescent nanoparticles and silver nanoparticles for effectively delivering noscapinoids to tumor cells. In conclusion, noscapinoids may be transformed to clinically viable formulations by conquering existing challenges.