

## From Bench to Bed Side: Opium Alkaloid - Noscapine: A Potential Chemotherapeutic Agent

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At cellular level, cancer is a disease of the cell that develops because of failures in the mechanisms that regulate cell growth. An individual cell multiplies without restraint until it and its progeny eventually overwhelm tissues and organs. Cancer development is a multistep process in which the summation of events is required to produce malignant tumor. Although there is tremendous progress in understanding the molecular events that lead to malignancy, progress in the development of clinically innovative drugs that can cure cancer is not moving at that pace.

A recent discovery that might challenge the existing knowledge of cancer and methods to treat it, researchers found that “cancer cells spread to organs much earlier than was thought.” In fact, cancer cells can spread even before a tumour develops, remain quiet for long periods of time and then awaken to form aggressive and fatal metastasis. The findings also offer an explanation for why some 5% of cancer patients have metastases but no original tumour. Cancer cells are able to spread from a nascent tumor much earlier than scientists long thought and are more adept than later emigrants at forming potentially lethal metastases at distant sites such as the brain and bones.

Chemotherapy with cytotoxic anticancer agents is still the main way of therapy targeted at specific cellular mechanisms in the malignant tissues. Some chemotherapeutic agents disrupt the crucial parts of the cell that are critical for cell division such as mitotic spindle. Most common cancers require combination of radiation and chemotherapy for the treatment.

Noscapine is a very safe cough suppressant (antitussive) which has been in use for many decades. In recent years, noscapine's anti-cancer effect has been demonstrated when taken at doses higher than those used for cough suppression. It is currently in off-label use by a number of physicians in treatment of cancers of the breast, lung, prostate, ovaries and brain, and lymphomas, to name but a few. It is being clinically studied in non-Hodgkin's lymphoma and chronic lymphocytic leukemia (CLL). Noscapine, a non-addictive derivative of opium, has also demonstrated outstanding clinical effectiveness in reducing death rates from strokes. Its long safety record, widespread availability and ease of administration make it an ideal candidate for fighting several life-threatening conditions.

Our laboratory established that noscapine inhibits the progression of cancer cells by interfering with microtubular functions at the cellular level and induces apoptosis as like taxanes and the vinca alkaloids. Noscapine binds to tubulin and alters its conformation, resulting in a disruption of the dynamics of microtubule assembly (by increasing the time that microtubules spend idle in a paused state) unlike other tubulin inhibitors such as taxanes and vinca alkaloids which affect microtubule polymerization. Perhaps more importantly, noscapine was able to inhibit cancer at doses (300mg/kg body weight) which produced little or no toxicity, including no adverse effects on the primary immune response. In addition, noscapine also demonstrated potential anti-angiogenic activity as an alternate anti-cancer mechanism.

In our novel analogues of noscapine as well as developed nanoformulations like 9-bromo-noscapine loaded human serum albumin nanoparticles, noscapine bearing rapid release solid lipid nanoparticles, noscapine and 9-bromo-noscapine loaded optimized liposomes and niosomes have shown promising consequences in in vitro and in vivo setup. Further, in depth in vivo investigations are needed on these optimized nanoformulations of noscapine and 9-bromo-noscapine, for translating in to the clinical viable anticancer products.

### Biography:

Prof. Ramesh Chandra is an outstanding scientist, revered teacher and an exceptionally successful administrator, who excels in institution building and eminently suited to provide leadership role in higher education. He is currently heading Department of Chemistry, University of Delhi, where he is serving as Professor for the last more than 26 years and Founder Director of Dr. B. R. Ambedkar Center for Biomedical Research, University of Delhi, since March 1991. He has been Vice-Chancellor, Bundelkhand University, Jhansi for six years (1999-2005); Member, Planning Commission, Government of U.P, India as well as the President of the Indian Chemical Society (2004-2006).

Professor Chandra shows deep commitment to the cause of higher education and research and possess in ample measure, quality of dynamic leadership and a vision required for building academic institutions and first rate researcher in the field of Biomedical Science. Professor Chandra started his research career at the



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October 01, 2020 | Virtual Conference

University of Delhi, thereafter he went to The New York Hospital-Cornell University Medical Center and the Rockefeller University, New York; State University of New York at Stony Brook, USA as Assistant Research Professor. He conducted advanced research at the Harvard University Medical School-Massachusetts General Hospital, jointly at MIT, Cambridge, USA. Over the last 38 years, Professor Chandra has contributed largely in the field of Chemical Sciences and particularly in New Drug Discovery and Development as well as Drug Metabolism. His research work is being used in the development of drugs for Physiological Jaundice/ Neonatal Jaundice and development of naturally occurring chemotherapeutic agents for the treatment of Breast and Ovarian Cancers, and drugs for Diabetes and Hypertension. He has supervised large number of (84 Ph. D. and 10 M. Phil) Students, in all trained more than 100 research scholars, who are now occupying high positions internationally. He has to his credit several patents, published more than 300 original Scientific Research Papers/ Review Articles in International journals of repute and six of his internationally acclaimed scientific Books. He is sought after speaker at several top universities in the world.

Prof. Chandra is the recipient of several professional national/ international recognitions; these includes: Millennium Plaques of Honor (Life Time Achievement Award for Contribution in Science & Technology) by the Indian Science Congress Association (ISCA) for 2017-2018, Award of the Highest Honor of Soka University, Tokyo, Japan (2000); J William Fulbright Scholarship (1993); The Rockefeller Foundation USA-Biotechnology Career Award (1993); and several others.