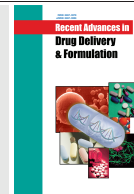




A Critical Appraisal of Lipid Nanoparticles Deployed in Cancer Pharmacotherapy



Santanu Chakraborty¹, Manami Dhibar¹, Aliviya Das², Kalpana Swain³ and Satyanarayan Pattnaik^{3,*}

¹Formulation Development Research Unit, Department of Pharmaceutics, Dr. B. C. Roy College of Pharmacy and AHS, Durgapur-713206, West Bengal, India; ²Calcutta Institute of Pharmaceutical Technology & AHS, Uluberia, Howrah, West Bengal, India; ³Division of Advanced Drug Delivery, Talla Padmavathi College of Pharmacy, Warangal, India

Abstract: Treatment modalities of various cancers and the delivery strategies of anticancer agents have evolved significantly in the recent past. The severity and fatality of the disease and hurdles to the effective delivery of therapeutic agents have drawn the attention of researchers across the world for proposing novel and effective drug delivery strategies for anticancer therapeutics. Attempts have been made to propose solutions to the diverse limitations like poor pharmacokinetics and higher systemic toxicities of the traditional delivery of anticancer agents. Nanotechnology-based drug delivery systems including lipid-based nanocarriers have demonstrated significant efficiency in this scenario. The review critically assessed the different types of lipid nanocarrier systems for the effective and optimal delivery of anticancer therapeutic agents. The diverse synthesis approaches are discussed for the laboratory scale and commercial development of different categories of lipid nanocarriers. Further, their application in anticancer drug delivery is illustrated in detail followed by a critical appraisal of their safety and toxicity.

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1. INTRODUCTION

Cancer is the world's second-biggest cause of death and treating it remains a serious problem as the number of cases rises. Patients with cancer are treated with a variety of methods, including surgery, chemotherapy, radiotherapy, and immunotherapy. Chemotherapy, on the other hand, may be the only way to improve survival odds once cancer has spread and become metastatic [1]. Except for breast cancer, which is treated with hormone treatment or immunotherapy, cytotoxic drugs are still the most common type of cancer chemotherapy. Anticancer drugs are usually cytotoxic agents which treat cancer by acting against the cancerous cells. These drugs preferentially target cancer cells because they frequently undergo fast growth and proliferation [2]. Despite decades of research, there are still significant unmet medical requirements in cancer detection and treatment. However, there are a large number of potentially effective therapeutic agents (both biopharmaceutical and small-molecule drug-related) that are either too large highly charged, unstable, and not too soluble to reach cancer target cells without the use of delivery "vehicles." [3]. The last few decades have witnessed a significant contribution of molecular biology in understanding cancer biology in a better

manner. This has paved the way for the development of therapeutic compounds that target the source of the problem: the molecular and cellular processes that lead to disease development. Unfortunately, many drug molecules are therapeutically ineffective due to diverse reasons including their poor aqueous solubility, and hence, require specialized delivery vehicles. In some cases, medications are unable to pass through cell membranes, resulting in insufficient concentrations at the target region. To overcome this, substantial pharmacological doses are required, resulting in side effects [4, 5]. To overcome this, Cancer nanotechnology has emerged as a cancer treatment method for anticancer medication delivery [6]. Nanomedicine has evolved as a viable technique not only for enhancing drug therapeutic index but also for overcoming biological obstacles over the last 20 years. Nanoparticles as drug delivery systems are made up of inorganic or organic components with diameters ranging from 1 to 1000 nanometres [7]. They can prevent chemotherapeutic drugs from degrading too quickly, extending their biological half-life. The first nanomedicines to be commercialized in cancer therapy were liposomes for parenteral delivery [8-11]. Polymeric micelles, or nanoscale supramolecular constructions made out of amphiphilic block copolymers, are proving to be effective drug delivery vehicles for lipophilic drugs [12]. Liposomes, which consist of one or more lipid bilayers encapsulating an aqueous core, are now the most popular nanoparticle drug delivery vehi-

*Address correspondence to this author at the Division of Advanced Drug Delivery, Talla Padmavathi College of Pharmacy, Warangal, India; Tel: +91-7386752616; E-mail: drsatyapharma@gmail.com