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DEVELOPMENT OF A STABLE FORMULATION DOXORUBICIN LIPOSOMAL INJECTION: BIOLOGICAL PERSPECTIVE

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ABSTRACT

The development of liposomal drug Formulations has revolutionized oncological therapeutics, offering targeted and controlled delivery systems that enhance efficacy while reducing systemic toxicity to the patients. Present research explores the innovative methodologies of Liposomal Doxorubicin. Hydrochloride employed by Biozenta Lifesciences Pvt. Ltd. a leading pharmaceutical enterprise renowned for its high-quality oncology formulations. One of the company's landmark innovations is the development of liposomal Doxorubicin, a chemotherapy drug encapsulated in lipid bilayers to improve pharmacokinetics. bioavailability, and patient outcomes. This formulation leverages advanced nanotechnology to encapsulate Doxorubicin, achieving remarkable drng stability and enhanced delivery to tumor sites via passive and active targeting mechanisms. The liposomal design minimizes cardio toxicity and myelosuppression, common adverse effects of traditional Doxorubicin therapy, while improving therapeutic efficacy. The Liposome formation was fixed by employing cutting-edge techniques such as high-resolution transmission electron microscopy (HR-TEM). dynamic light scattering, and HPLC analysis to confirm the particle lamellarity, size uniformity. and drug entrapment efficiency, achieving an impressive 98% encapsulation rate with nanoscale size (314.16 nm) and stable zeta potential (-0.5 mV) of the liposomes ensure effective tumor penetration and prolonged circulation time, enhancing drug efficacy.

KEYWORDS: Doxorubicin, Liposomes, HR-TEM, HPLC Analysis, Ultracentrifugation, Particle size.

1. INTRODUCTION

Liposomes are spherical vesicles composed of lipid bilayers, widely studied for their potential in drug delivery, cosmetics, gene therapy, and other biomedical applications. British biochemist Alec Bangham first described them in the early 1960s as a method of studying the properties of cell membranes (AD, 1960). Liposomes mimic the structure of biological membranes, with an aqueous core encapsulated by one or more lipid bilayers, allowing them to encapsulate both hydrophilic and hydrophobic substances. The unique structure of liposomes, an aqueous center entrapped in lipid bilayers, facilitates the chaperoning of various hydrophilic and hydrophobic therapeutic molecules such as phytochemicals, chemotherapeutic or immunotherapeutic agents, and RNA molecules for cancer therapy (Smith J, 2022).

Furthermore, using liposomes as nanocarriers for drug delivery would improve the pharmacokinetics of the loaded therapeutic molecules and prolong their half-lives (>72 h) via surface coating with polyethylene glycol (PEG) (Doe J, Liposomes as nanocarriers: Enhancing drug delivery and pharmacokinetics, 2023).

1.1 Liposomal Drugs

Liposomal drugs use liposomes as carriers to enhance the delivery and efficacy of therapeutic agents. Liposomes are spherical vesicles composed of lipid bilayers that can encapsulate various drugs, including anticancer agents, proteins, and nucleic acids.

Advantages of Liposomal Drugs

1. Improved Drug Stability.
2. Controlled Release
3. Targeted Delivery
4. Biocompatibility
5. Bioavailability
6. Versatility
7. Reduced Toxicity

1.2 Doxorubicin

Doxorubicin is a cytotoxic anthracycline antibiotic isolated from cultures of Streptomyces peucetiusvar caesiusalong side with adaunorubicin, another cytotoxic agent, in 1970 (Nicolini A, .2003). Although they both have aglyconic and sugar moieties, doxorubicin's side chain terminates with a primary alcohol group compared to the methyl group of daunorubicin (Dunlap NE, 2006). Owing to its effectiveness and broad effect, The FDA authorized doxorubicin in 1974 (Harris L, 2006). To treat

a variety of cancer, including but not limited to breast, lung, gastric, ovarian, thyroid, non-Hodgkin's and Hodgkin's lymphoma, multiple myeloma, sarcoma, and pediatric cancers (U.S.FDA)

1.3 Objective of the research

The aim is to improve the stability by focusing on designing drugs that are more specific against cancer cells and affordability for patients.

2. MATERIAL AND METHODS

2.1 Materials for Preparation of Doxorubicin Liposomes

DSPC, cholesterol (CHOL), and mPEG-DSPE were among the lipids that were kept at -20°C and allowed to come to room temperature prior to being weighed. It was necessary to handle the cytotoxic drug doxorubicin carefully while wearing gloves and a mask when weighing it.[8] A citrate solution (pH 4.0, 0.3 mol/L) was created by dissolving sodium citrate, or citric acid, in deionized water and then kept at room temperature to create the hydration buffer. By dissolving sodium carbonate in deionized water, a sodium carbonate solution (0.5mol/L) was created that was utilized to modify the external pH of liposomes. Among the other reagents was 0.9% sodium chloride. The method made use of a high-pressure homogenizer, like the EmulsiFlex-C5, to prepare and refine liposomes effectively. (Kumar A, 2017).

2.2 Method of Preparation of Doxorubicin Liposome:

Phospholipids (HSPC) and cholesterol (MPEG-DSPE) are dissolved in an organic solvent (chloroform) and then evaporated to form a thin lipid film in order to make doxorubicin HCl liposomal injection. For the purpose of producing multilamellar vesicles (MLVs), hydrate the film with an aqueous buffer at 50 to 60°C. To optimize loading using methods like pH modification or ion gradients, combine doxorubicin HCl with L-Histidine, Ammonium Sulphate, and Sucrose in an ethanol solvent and thoroughly mix with the liposomal suspension for encapsulation in a homogenizer. To create homogenous liposomes, use a high-pressure homogenizer to reduce the particle size (100–500 nm). (Ghosh P, 2012) After sterilizing with a 0.22 µm filter, set the pH to 4.5–5.5 and dilute with sterile water to the appropriate concentration for injection. Using the proper tests to ensure sterility, stability, and quality, aseptically package into vials and store at 2–8°C with light protection. (Rosenblum D, 2018).

3. RESULT AND DISCUSSION

1. Lamellarity

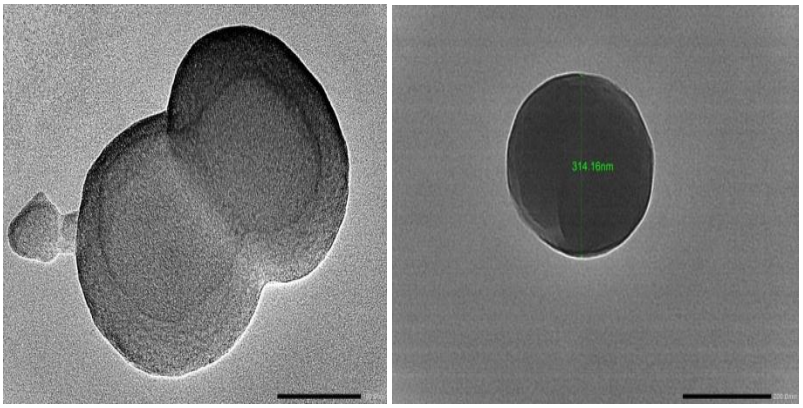
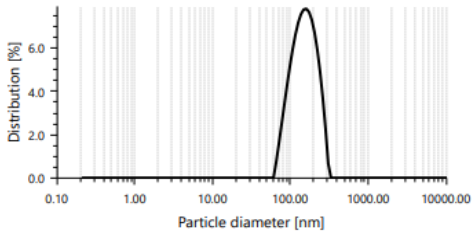


Figure 2(a) and (b): TEM images of Doxorubicin liposome.

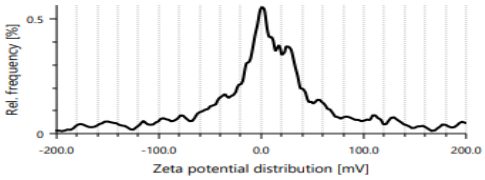
2. Particle Size Distribution



Result

Hydrodynamic diameter	152.27 nm	**Mean intensity**	301.6 kcounts/s
Polydispersity index	21.0 %	**Absolute intensity**	951196.6 kcounts/s
Diffusion coefficient	3.2 µm²/s	**Intercept g1²**	0.8631
Transmittance	15.5 %	**Baseline**	0.998

3. Zeta Potential

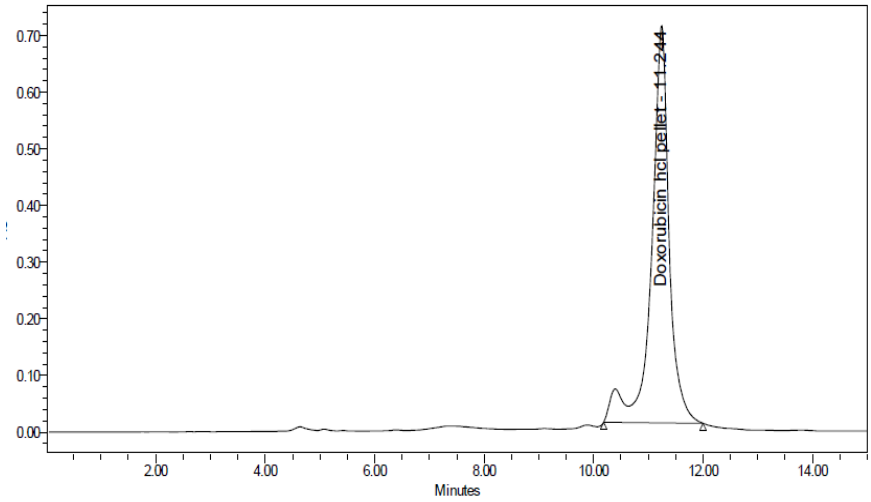


Result

Mean zeta potential	-0.5 mV	**Mean intensity**	15.6 kcounts/s
Standard deviation	4.7 mV	**Filter opical density**	0.0000
Distribution peak	0.7 mV	**Conductivity**	0.111 mS/cm
Electrophoretic Mobility	-0.0428 µm*cm/Vs	**Transmittance**	0.3 %

4. Ultracentrifugation

5. Drug Entrapment



	Peak Name	RT	Area	% Area	Height
1	Doxorubicin hcl pellet	11.244	15865832	100.00	702021

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