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FORMULATION OF LIPOSOMES LOADED WITH CIPROFLOXACIN HYDROCHLORIDE BY THE ETHANOL INJECTION METHOD

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Abstract

Objective: This study aims to develop and characterize lipidic vesicles highly loaded with ciprofloxacin hydrochloride (CPX-HCL) obtained by ethanol injection method.

Materials and Methods: Six formulations of liposomes were developed by the ethanol injection technique. Lipoid S75 was utilized at concentrations ranging from 40 to 100 mg/ml, while cholesterol was incorporated at concentrations between 10 and 15 mg/ml. CPX-HCl concentration was maintained at 3.5 mg/ml across all formulations. The process was conducted at 50°C, with an injection flow rate of 0.6 ml/min. Each formulation was characterised based on these parameters: encapsulation efficiency (EE), particle size, particle distribution index, pH, morphology and physical stability. A microbiological efficacy test was conducted on reference strains of pseudomonas aeruginosa. Stability studies (Ph and EE) conducted at 10°C, abated from light.

Results: Dynamic Light Scattering analysis of liposomal suspension revealed different particle sizes ranging from 229.2 nm to 797.8 nm, and varying polydispersity indexes from 0.471 to 0.967 (in terms of light intensity). Among all formulations, F3 presented the best granulometric results and the smallest mean diameter. Conversely, F4 exhibited the largest vesicle diameter (797.8 nm). The EE varied from 39.01% (F6) to 97.56% (F4). The microscopic analysis showed unilamelar vesicles for all formulations. According to liposome classification, F3 corresponds to Small Unilamellar Vesicles (SUVs), whereas F4 aligns with the Large Unilamellar Vesicles (LUVs). Formulations pH values varied from 6.5 to 5.5.
After 14 days, F4 showed unchanged characteristics. Unfortunately, F3 exhibited a reduction in EE percentage to below 5%. When compared to free CPX-HCl solution, microbiological assays revealed that both F3 and F4 enhanced the CPX antibacterial activity against Pseudomonas aeruginosa, as evidenced by the largest inhibition zones. In the same conditions, the corresponding placebos didn't express any antibacterial effect.

Conclusion: This study emphasizes the potential of liposomes as effective carriers for Ciprofloxacin nanoencapsulation, significantly improving its antibacterial efficacy, and suggests that Ciprofloxacin-liposomes could provide a promising approach for the management of infections affecting ocular, cutaneous, and respiratory pathways.

Keywords: Drug delivery, ethanol injection, liposomes, pseudomonas aeruginosa, vesicles.

1. INTRODUCTION

- Ciprofloxacin hydrochloride (CPX-HCl) is an effective drug for treatment of infectious diseases; however, its clinical efficacy is hindered by low bioavailability across various administration routes.
- The need for frequent dosing to achieve therapeutic levels can lead to patient non-compliance and potential side effects(1,2).
- Liposomal formulations of CPX-HCl present an innovative strategy to enhance drug delivery, improve stability, and mitigate toxicity (2).

Objective

❖ This study aims to develop and characterise lipid vesicles with a high efficacy of encapsulation (EE) for CPX-HCl.

2-MATERIAL AND METHOD

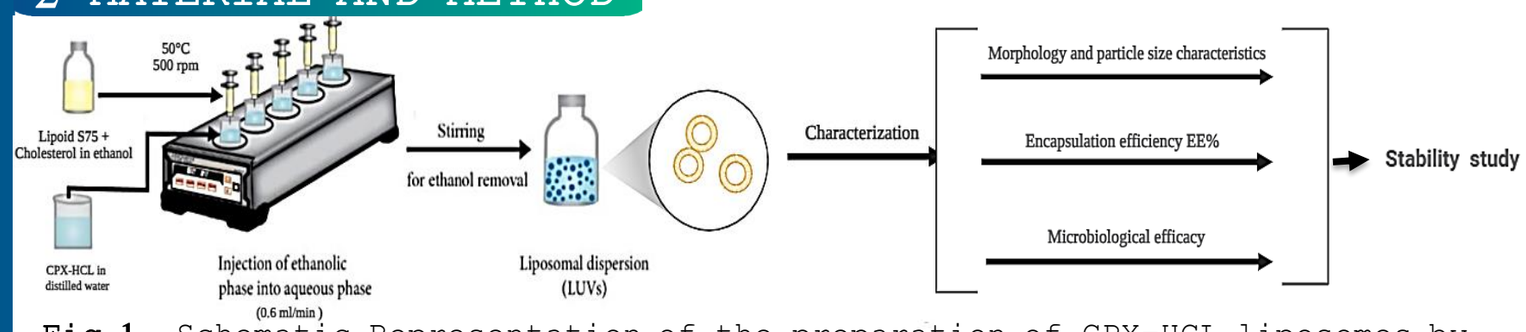

Fig 1. Schematic Representation of the preparation of CPX-HCL liposomes by the ethanol injection method.

Table 1. Liposomal formulae composition

Proportion / Formula	Lipoid S75 (mg/ml)	Cholesterol (mg/ml)	phase ratio Organic /aqueous	CPX-HCL (mg/ml)
F01	40	10	1:10	3.5
F02	40	15	1:10	3.5
F03	60	10	1:10	3.5
F04	60	15	1:10	3.5
F05	100	10	1:10	3.5
F06	100	15	1:10	3.5

3-RESULTS AND DISCUSSION

Table 1. Results of Particle Size, EE, pH, and Stability of all formulations

Results / Formula	Z avg (nm)	PDI	EE%	pH	Stability (days)
F01	375.2	0.590	41.32	5.63	7
F02	343.7	0.967	81.21	6.27	7
F03	229.2	0.471	97.18	6.43	14
F04	797.8	0.619	97.56	6.50	30
F05	577.0	0.671	92.93	6.38	3
F06	678.0	0.556	39.01	5.50	3

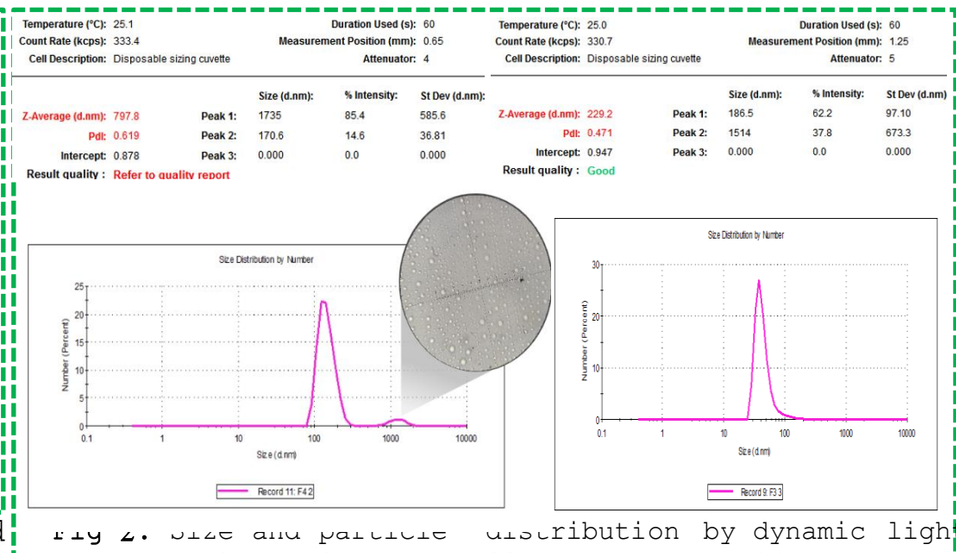

Fig 2. Size and particle distribution by dynamic light scattering; Liposome: f03 (right) and f04 (left).

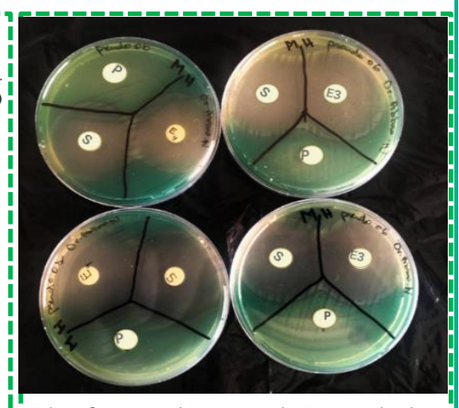

Fig 3. antibacterial activity of the pure drug (S) and CPX-HCL Liposomes (E3 for F3 and E4 for F4) and their corresponding Placebos against *Pseudo.aeruginosa*.

- This study demonstrating that high phospholipid concentrations lead to larger particle sizes and enhanced EE (3).
- Incorporating cholesterol significantly increases liposome diameter by disrupting the phospholipid bilayer, enhancing membrane fluidity, and promoting uniform aqueous phase distribution(4).
- F4 exhibited superior physical stability over 30 days at 10°C, suggesting a correlation between vesicle size and structural integrity during storage.
- The results indicate the effective encapsulation of CPX, consistent with previous studies on solid lipid microparticles (SLM) of CPX-HCL(5).

4-CONCLUSION

This study illustrates the efficacy of liposomes as carriers for ciprofloxacin nanoencapsulation, significantly enhancing its antibacterial potency and indicating their potential application in treating ocular, cutaneous, and respiratory infections.

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