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RESEARCH

Formulation and Development of Ligustrazine-Loaded Liposomes: A promising Drug Repurposing Approach for treating Nephrotoxicity

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Abstract

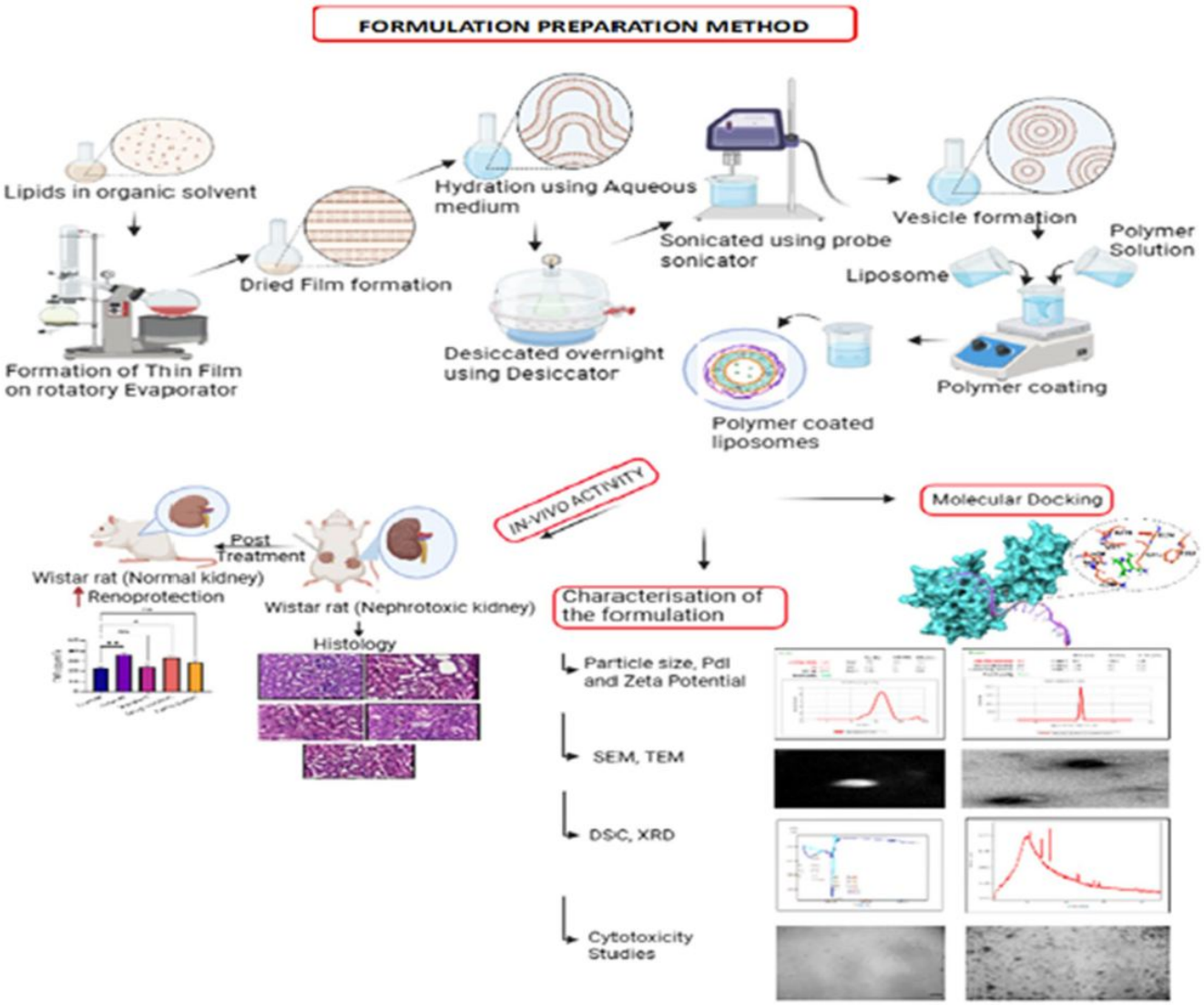
Nephrotoxicity occurs when the kidneys are harmed by chemicals, toxins, or drugs, potentially leading to chronic kidney disease and impaired function. Ligustrazine liposomes were created using the thin-film hydration method. The best batches were tested for particle size, polydispersity index, zeta potential, drug release, entrapment efficiency, and morphology assessed by SEM and TEM. DSC and X-RD confirmed the drug's thermal stability and amorphous form. These liposomes were then coated with an optimal amount of polyethyleneimine and evaluated using the same parameters. The polyethyleneimine-coated Ligustrazine liposomes measured 152.8 nm in size, had a polydispersity index of 0.314, a zeta potential of 14.4 mV, and an entrapment efficiency of 93%, with 72% drug released after 24 h. A nephroprotective effect comparison was made by administering 1 g/kg of acetaminophen orally to male Wistar rats. In vivo results indicated that polyethyleneimine-coated Ligustrazine liposomes protect against chemically induced nephrotoxicity, while docking studies showed a comparatively favorable predicted interaction of Ligustrazine with sEH (PDB ID: 3ANS; docking score: −5.184 kcal/mol) and a weak, suggestive interaction with NF-κB (PDB ID: 1SVC; docking score: −1.744 kcal/mol). MTT assays confirmed that the coated liposomes are non-toxic at higher concentrations in kidney tissues. Overall, these polyethyleneimine-coated Ligustrazine liposomes are a promising option for treating nephrotoxicity.

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Graphical Abstract



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1 Introduction

As the body's most crucial excretory organ, the kidney is particularly vulnerable to chemical and pharmacological toxicity [1]. It also plays a crucial role in human physiology by regulating blood pressure and erythrocyte formation, excreting nitrogenous waste products, and more [2–4]. Nephrotoxicity remains a major clinical problem and can lead to acute kidney injury (AKI) or chronic kidney disease (CKD), both of which continue to impose a substantial global health burden. In particular, acetaminophen-induced renal injury is closely associated with oxidative stress, inflammation, and apoptosis, making it a suitable model for evaluating protective therapies [5–7]. Both CKD and AKI have arisen globally and are recognized as significant public health issues, and CKD is projected to be the fifth leading cause of death worldwide by 2040 [8]. Several medicines are available, but they are less effective because of pharmaceutical limitations and toxicity. Herbal traditional medicines have been used extensively to treat various ailments since the medieval period, including liver conditions. In recent years, research has focused more on herbal constituents due to their multi-targeted protective effects against nephrotoxicity—reducing oxidative stress, inflammation, apoptosis, and fibrotic pathways—often with fewer adverse effects than some synthetic agents [9, 10]. However, their