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α-Tocopherol succinate Nanostructured Lipid carriers for the Ocular delivery of the anti-neoplastic agent

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i. Project Summary

Overview: Retinoblastoma (RB) is a rare form of cancer that rapidly develops from the immature cells of the retina, the light-detecting tissue of the eye. The treatment options of RB has been limited to enucleation, external beam radiotherapy, episcleral plaque radiotherapy and cryotherapy. α-Tocopherol succinate (αTS), has been proven to an effective apoptogenic agent. It can enhance the efficiency of the anticancer agent[1]. Paclitaxel (Ptx) is a potent chemo agent and is widely used in the treatment of various types of cancers. However, clinical use of Paclitaxel is limited by systemic toxicity, rapid clearance and resistance[2,3]. The formulation of paclitaxel poses the challenge of incorporation of drug in a Chremophor free and organic solvent free matrix. Moreover, the blood-retinal barrier also limits the potential of Ptx. αTS and Ptx when combined together can exert a synergistic effect, thus increasing the efficiency while reducing the required dose of the anti-cancer agent.

Intellectual Merit: Paclitaxel a taxane compound, originally derived from the bark of Pacific yew is extensively researched and used in treatment of various types of cancers[2]. Paclitaxel acts by binding and inactivating the intracellular proteins necessary for cell survival and functioning, thus including cell death[3,4]. αTS is a succinic acid ester form of Vitamin E, a variate more stable than the α-tocopherol[1]. The normal cells can hydrolyze the αTS to the original α-tocopherol, while the cancer cells lack the machinery to convert the ester to the original form, resulting in the cytotoxic activity of α-TS. Thus, this mechanism can be implemented along with Ptx for anticancer therapy.

The conventional methods of treatments in retinoblastoma consists of systemic delivery of the chemotherapeutic agents leading to severe side effects and decreased bioavailability[5]. The delivery of drugs by the ocular routes can help overcome this challenge along with advantages such as ease of administration, increased precorneal residence time and enhancement in ocular bioavailability of drugs[6]. The NLCs can be pass through the corneal barriers as well as they can deliver the drug to the posterior section of eye[7]. The controlled release of Paclitaxel from the NLC will ensure that therapeutic levels of drugs are maintained at the site of action. This will reduce the amount of drug required to induce the cytotoxic action. Thus, Paclitaxel and α-Tocopherol succinate together can show synergistic activity. The FDA approved paclitaxel formulation constitute paclitaxel in Chremophor EL and Ethanol. Due to the inherent toxicity of Chemophor and deleterious effects of ethanol on eye[8,9], this formulation cannot be used for ocular drug delivery. Hence, the objective of this study was to formulate paclitaxel delivery system, without chemophor or any organic solvent.

External Funding Opportunities –

The data from the project will be used by the institution for the following grant application

Sponsor – National Institutes of Health (NIH)

Title - NCI Small Grants Program for Cancer Research for Years 2020, 2021, and 2022 (NCI Omnibus R03 Clinical Trial Optional)

Funding Opportunity Number: PAR-20-052

Funding amount - $50000

Application Due Date - Jan 07, 2023

This funding opportunity will help advance the nano-formulations in cancer treatment and will also help me have project funded from my data. This opportunity will be a boost to seek a future position as a scientific researcher.