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Vitamin-based nanomicelles for improved paclitaxel therapy

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Pancreatic cancer remains one of the most feared diseases worldwide due to its poor prognosis and high mortality rate [1]. Paclitaxel is one of the most effective chemotherapeutic drugs approved for pancreatic cancer treatment. However, its current clinical outcomes are limited by its low solubility, large molecular weight, severe systemic toxicity, and multiple drug resistance (MDR) development [2]. Nanotechnology-driven therapeutics constitute a promising strategy to enhance the safety and efficacy of paclitaxel, enabling its encapsulation, protection, controlled release, and reduction of off-target toxicity [3]. The present work focuses on developing multifunctional vitamin-based nanomicelles for paclitaxel delivery with lower systemic toxicity and enhanced therapeutic efficacy. Nanomicelles were prepared by the solvent evaporation method. The mean particle size, polydispersity index, and zeta potential of prepared PTX-loaded nanomicelles were determined using dynamic light scattering and electrophoretic light scattering. Morphological evaluation of the prepared nanomicelles was carried out by transmission electron microscopy (TEM). The stability of vitamin-based nanomicelles was evaluated by monitoring the particle size upon storage at 4°C protected from light for a month. All prepared vitamin-based micelles were stable and presented a spherical morphology, an average particle size of less than 100 nm, a monomodal particle size distribution, and a zeta-potential close to neutrality, and a high encapsulation efficiency being promising drug delivery systems to improve paclitaxel distribution, penetration, and tumor accumulation in poorly permeable tumors such as pancreatic cancer. Overall, vitamin-based nanomicelles were successfully prepared and characterized, constituting a promising therapeutic approach toward safer and more effective pancreatic cancer treatment.

Introduction:

Pancreatic cancer remains one of the most feared diseases worldwide due to its poor prognosis and high mortality rate [1]. Paclitaxel is one of the most effective chemotherapeutic drugs approved for pancreatic cancer treatment. However, its current clinical outcomes are limited by its low solubility, large molecular weight, severe systemic toxicity, and multiple drug resistance (MDR) development [2]. Nanotechnology-driven therapeutics constitute a promising strategy to enhance the safety and efficacy of paclitaxel, enabling its encapsulation, protection, controlled release, and reduction of off-target toxicity [3].

Objectives:

The present work is focused on the development and characterization of multifunctional vitamin-based nanomicelles for paclitaxel delivery with lower systemic toxicity and enhanced therapeutic efficacy.

Materials and Methods:

Novel amphiphilic vitamin-based conjugates comprising the hydrophilic FDA-approved polyethylene glycol combined with a hydrophobic vitamin bearing intrinsic MDR reversal and anticancer properties were synthesized to produce vitamin-based micelles by the solvent evaporation method. The mean particle size, polydispersity index (PDI), and zeta potential of prepared blanck micelles and PTX-loaded nanomicelles were determined using dynamic light scattering (DLS) and electrophoretic light scattering (ELS). Morphological evaluation of the prepared nanomicelles was carried out by transmission electron microscopy (TEM). Encapsulation efficiency was investigated using a validated HPLC-UV method. Long-storage stability of vitamin-based nanomicelles was evaluated by monitoring the particle size upon storage at 4°C protected from light for a month. Additionally, colloidal stability of vitamin-based nanomicelles was assessed in biorelevant media to mimic the physiological environment after intravenous administration.

Results:

All prepared vitamin-based micelles presented minimal batch-to-batch variation with an average particle size less than 100 nm and a monomodal particle size distribution (PDI up to 0.2), being promising drug delivery systems to improve paclitaxel distribution, penetration, and tumor accumulation in poorly permeable tumors such as pancreatic cancer. Additionally, vitamin-based micelles exhibited a zeta-potential close to neutrality confirming the presence of PEG chains in the shell of the nanomicelles. The morphology of the nanomicelles studied by TEM revealed that amphiphilic vitamin conjugates were able to readily self-assemble to form spherical micelles. The encapsulation efficiency of paclitaxel was higher than 50%. Stability studies showed that vitamin-based nanomicelles physicochemical properties remain unaltered in the presence of biorelevant media and over the period of a month at 4 °C, indicating good stability.

Conclusion:

Overall, vitamin-based nanomicelles were successfully prepared and characterized, being a promising therapeutic approach toward a safer and more effective pancreatic cancer treatment.