Development of a Stimuli-responsive Nanocarrier for Prostate Cancer Treatment

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Introduction

Prostate cancer (PCa) is characterized by overexpression of monoamine oxidase-A (MAO-A), which promotes tumor growth, and metastasis. Consequently, repurposing MAO inhibitors like phenelzine for PCa management has emerged as a promising strategy. However, preliminary research indicates that systemic administration of phenelzine at doses effective for anti-tumor activity cause central nervous system side effects. Therefore, there is a need to develop a drug delivery platform that can precisely transport phenelzine to PCa cells.

Methods

Polyethylene glycol-hydrazone-phenelzine (PEG-HZ-PHE) was synthesized by reacting PEG_{2000}-aldehyde and phenelzine in a 1:5 mole ratio in anhydrous methanol. The formed product (PEG-HZ-PHE) was used in the formulation of stimuli-responsive nanocarriers and characterized according to the Figure 1 below.

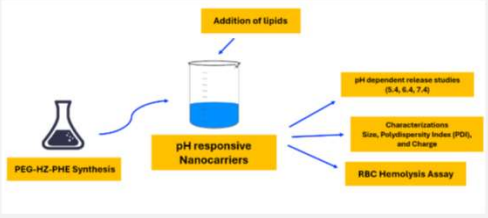

Figure 1: Procedural flow of methods used during experiment

Results and Discussions

The pH-responsive nanocarriers demonstrated a particle size of 168.9 ± 1.595 nm and polydispersity index (PDI) of 0.16 ± 0.02. From the pH dependent release study, it was observed that at 18 h, phenelzine release was highest at pH 5.4 (74.70%) and lowest at pH 7.4 (11.30%). The nanocarriers effectively release phenelzine in acidic environments, making them ideal for targeted drug delivery to sites like the tumor microenvironment which is characterized by an acidic pH. The red blood cells (RBCs) hemolysis assay showed no significant difference in the hemolytic activity of the formulation compared to the negative control (phosphate buffered saline). This indicates that the drug delivery system is safe, as it does not induce harmful RBC lysis.

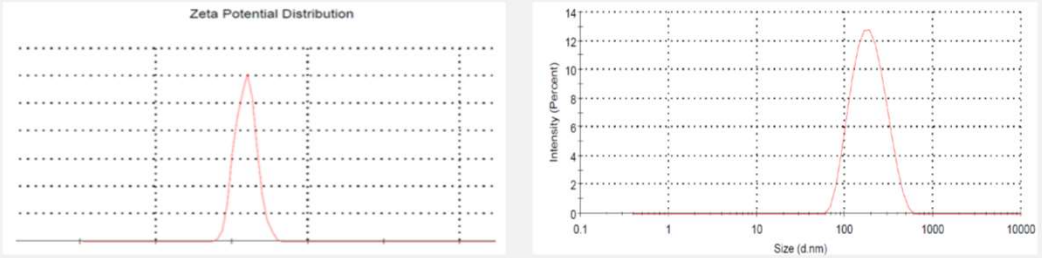

Figure 2: Dynamic light scattering (DLS) analysis showing (A) Size distribution and (B) surface charge of the pH responsive nanocarrier

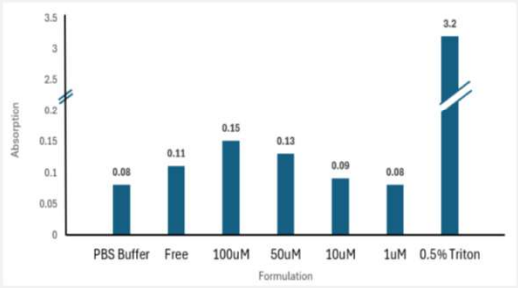

Figure 3: Hemolysis Assay of pH-responsive nanocarriers

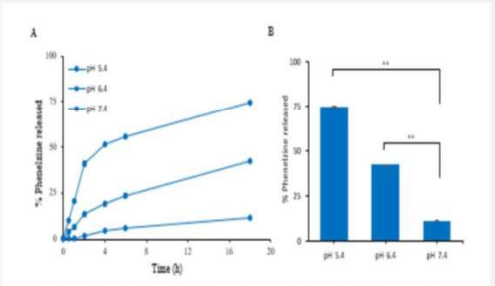

Figure 4: Phenelzine release from the formulation at pH 5.4, 6.4 and 7.4 (A) over a period of 0-18 h and (B) at 18 h of incubation in 0.1M Tris buffer.

Formulation	Size	PDI	Zeta
Plain	162.2 ± 3.092	0.175 ±0.014	-32.2 ± 0.436
Hydrazone	168.9 ± 1.595	0.155 ± 0.021	-41.7 ± 1.83

Table 1: Chart and table showing characterization values and size distribution of nanoparticles.

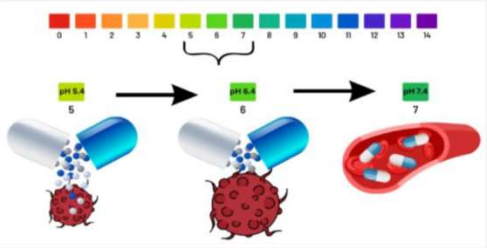

Figure 5: Schematic representation of drug release under different pH conditions.

Conclusions

We have developed a pH-responsive nanocarrier that is stable at physiological pH (i.e., pH 7.4) but is rapidly hydrolyzed in acidic environment (pH 5.4 and 6.4). This formulation did not exert any gross hemolytic activity against RBCs.

References

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