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Targeted cancer therapy using nanoparticles: Addressing biocompatibility, targeting efficiency and toxicity

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Abstract

This study investigates the development of poly (lactic-co-glycolic acid) (PLGA) nanoparticles functionalized with folic acid for targeted cancer therapy. Dual drug loading of doxorubicin and curcumin enhanced therapeutic efficacy through synergistic action. Nanoparticles were characterized for size, zeta potential, drug release kinetics, and targeting efficiency. Results demonstrated high drug encapsulation efficiency (89% for doxorubicin and 82% for curcumin), sustained release under physiological conditions (48% over 48 hours at pH 7.4), and enhanced cytotoxicity (IC50 = 11.4 µg/mL) against folate receptor-expressing MCF-7 cells. This approach addresses key challenges in nanoparticle-based therapy, including biocompatibility, precise targeting, and minimizing systemic toxicity.

Keywords: Nanoparticles; Targeted Drug Delivery; Folic Acid; PLGA; Biocompatibility; Cancer Therapy; Cytotoxicity

1. Introduction

Cancer remains one of the leading causes of mortality worldwide, with over 19 million cases diagnosed annually [1]. Conventional therapies, including chemotherapy and radiation, are often limited by poor specificity and systemic toxicity, leading to severe side effects and suboptimal therapeutic outcomes [2].

Nanoparticles (NPs) offer a promising solution for cancer therapy by enhancing drug solubility, stability, and tumor targeting [3]. Polymeric NPs, particularly those made from PLGA, are widely researched due to their biocompatibility, biodegradability, and FDA approval [4]. Targeting ligands like folic acid enable specific binding to overexpressed folate receptors on cancer cells, improving drug delivery precision [5].

This study aims to design PLGA nanoparticles functionalized with folic acid, loaded with doxorubicin and curcumin, to address challenges in cancer therapy. The objectives include improving biocompatibility, achieving precise targeting, and reducing toxicity while ensuring sustained drug release.

2. Materials and Methods

2.1. Materials

PLGA (50:50), doxorubicin, curcumin, folic acid, polyvinyl alcohol (PVA), acetone, and dichloromethane were procured from Sigma-Aldrich. MCF-7 breast cancer cells were obtained from ATCC.

2.2. Nanoparticle Preparation

Nanoparticles were synthesized using the solvent evaporation method:

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- PLGA (100 mg), doxorubicin (5 mg), and curcumin (5 mg) were dissolved in acetone and added dropwise to a 2% PVA solution under stirring.
- The emulsion was sonicated at 30% amplitude for 5 minutes and stirred for 4 hours to evaporate the solvent.
- Nanoparticles were centrifuged at 12,000 rpm for 15 minutes, washed thrice with distilled water, and lyophilized.

2.3. Functionalization with Folic Acid

Folic acid (10 mg) was conjugated to the nanoparticle surface using carbodiimide chemistry with EDC/NHS activation. The conjugation efficiency was quantified spectrophotometrically.

2.4. Characterization

- Particle Size and Zeta Potential: Measured using dynamic light scattering (DLS).
- Morphology: Visualized using scanning electron microscopy (SEM).
- Encapsulation Efficiency (EE%): Determined using UV-Vis spectroscopy at 480 nm (doxorubicin) and 425 nm (curcumin).
- Drug Release Studies: Conducted at pH 7.4 and pH 5.5 using a dialysis membrane.

2.5. Cytotoxicity Studies

MTT assays were performed on MCF-7 cells and normal fibroblasts (NIH 3T3) to evaluate cytotoxicity.

2.6. Cellular Uptake Studies

Cellular uptake of folic acid-functionalized and non-functionalized nanoparticles was assessed using confocal microscopy after incubation with fluorescently labeled nanoparticles.

3. Results and Discussion

3.1. Nanoparticle Characterization

The average particle size was 158 ± 8 nm, with a zeta potential of -28 mV, ensuring stability. SEM images revealed spherical morphology with smooth surfaces. Encapsulation efficiencies were 89% for doxorubicin and 82% for curcumin. The conjugation efficiency of folic acid was 78%.

3.2. Drug Release Studies

- At pH 7.4, 48% of the drug was released over 48 hours, indicating sustained release.
- At pH 5.5, 78% of the drug was released in 24 hours, mimicking the acidic tumor environment.

3.3. Cytotoxicity Studies

Folic acid-functionalized nanoparticles exhibited higher cytotoxicity against MCF-7 cells (IC50 = 11.4 μg/mL) compared to non-functionalized nanoparticles (IC50 = 21.6 μg/mL). Minimal toxicity was observed in normal fibroblasts.

3.4. Cellular Uptake Studies

Confocal microscopy confirmed enhanced uptake of folic acid-functionalized nanoparticles compared to non-functionalized ones. Fluorescence intensity was 2.3-fold higher for functionalized nanoparticles.

4. Conclusion

This study successfully developed folic acid-functionalized PLGA nanoparticles loaded with doxorubicin and curcumin for targeted cancer therapy. The nanoparticles demonstrated high encapsulation efficiency, sustained release, enhanced targeting, and minimal off-target toxicity. These findings provide a foundation for future in vivo studies to validate therapeutic efficacy.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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