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Evaluation of the Biocompatibility and Cytotoxic Potential of Carbon Dot Nanoparticles Using Controlled In Vitro Studies

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Abstract

Cancer continues to be one of the leading causes of mortality worldwide, with conventional chemotherapy often resulting in severe side effects that compromise patient quality of life. In recent years, nanoparticle-based approaches have gained attention for their potential to deliver therapeutic agents directly to cancer cells while minimizing systemic toxicity. Among these, carbon-based nanoparticles, specifically carbon dots (C-dots), offer significant advantages due to their biocompatibility and low toxicity compared to metallic nanoparticles, yet their application in oncology remains relatively underexplored. In this study, carbon dots were synthesized through a simple one-step wet chemical method using three carbohydrate precursors: glucose (GCD), sucrose (SCD), and fructose (FCD). The resulting nanoparticles were characterized using UV-Visible and fluorescence spectroscopy to confirm their structural and optical properties. The anticancer potential of these C-dots was evaluated against human liver carcinoma (HepG2) and human breast carcinoma (MCF-7) cell lines using the MTT assay. The IC_{50} values determined for HepG2 cells were 67.24 µg/mL for SCD, and less than 50 µg/mL for both GCD and FCD, while for MCF-7 cells, the IC_{50} values were 105 µg/mL for SCD and below 50 µg/mL for GCD and FCD. These findings demonstrate that C-dots synthesized from different sugar precursors can effectively inhibit cancer cell growth, highlighting their potential as novel candidates for anticancer drug development and targeted therapy applications.

KEYWORDS: Carbon dot nanoparticles; Cytotoxicity; Anticancer activity; HepG2; MCF-7; Nanomedicine; SCD; GCD; FCD.

INTRODUCTION

Cancer remains one of the leading causes of death globally, driving the urgent need for innovative therapeutic strategies. Recent advances in nanotechnology have highlighted the potential of nanomaterials as multifunctional agents capable of targeting tumors, delivering drugs, and monitoring therapeutic outcomes simultaneously. While metal nanoparticles, such as zinc oxide and silver, have been widely investigated for their anticancer properties, concerns about toxicity and biocompatibility persist. In contrast, non-metallic nanomaterials, particularly carbon-based nanoparticles like carbon dots (C-dots), are emerging as promising alternatives due to their low toxicity, biocompatibility, and versatile functionalization potential [1].

Carbon dots are ultra-small carbon nanoparticles, typically less than 10 nm in size, which can be chemically modified with various organic molecules to tailor their surface properties. These functionalized nanoparticles have shown potential for diverse biomedical applications, including bioimaging, drug delivery, and cancer therapy. For example, recent studies have demonstrated that carbon dot-supported atomically dispersed gold can act as a mitochondrial oxidative stress amplifier, providing a novel approach for cancer treatment. Unlike many conventional

nanoparticles, C-dots are water-soluble, environmentally friendly, and can be synthesized from abundant biological sources, thereby reducing both ecological impact and production costs [2].

The use of nanoparticles as biological probes has already transformed cancer research, enabling sensitive and selective imaging of cells and tissues. Materials such as gold nanoshells, semiconductor quantum dots, iron oxide nanoparticles, carbon nanotubes, and polymer nanocarriers have been employed for in vitro and in vivo imaging and targeted therapy. However, many of these materials face limitations including poor aqueous solubility, photoinstability, low bio-distribution, and lack of target specificity, which restrict their therapeutic efficiency. Carbon dots, in comparison, offer an attractive platform for developing multifunctional nanomedicine systems that can overcome these shortcomings while maintaining biocompatibility and chemical stability.

The nanoscale properties of C-dots, including their high surface-to-volume ratio, facile surface functionalization, and unique optical and quantum characteristics, enable them to interact with biological systems in ways that conventional drugs cannot. Their small size allows cellular uptake, access to nuclear compartments, and targeted interaction with specific biomolecules such as proteins or nucleic acids. This makes C-dots highly suitable for applications ranging from drug delivery and cytotoxicity studies to advanced bioimaging.

In the present study, non-metallic carbon dots were synthesized via a simple wet chemical method using three different carbohydrate precursors: glucose, sucrose, and fructose. The synthesized nanoparticles were characterized using UV-Visible and fluorescence spectroscopy to confirm their optical properties. Their cytotoxic potential was evaluated against human liver carcinoma (HepG2) and human breast carcinoma (MCF-7) cell lines using the MTT assay, a colorimetric method that measures cell viability based on mitochondrial reduction of MTT to insoluble formazan crystals. The intensity of the resulting purple color correlates with the number of viable cells and can be quantified spectrophotometrically at 570 nm [3]. This investigation aims to explore the potential of carbon dots as non-toxic, multifunctional nanomaterials for anticancer applications, offering insights into their future use in targeted therapy, imaging, and nanomedicine.

MATERIALS AND METHODS

Cell Lines and Culture Medium

Human liver carcinoma (HepG2) and human breast adenocarcinoma (MCF-7) cell lines were obtained from the National Centre for Cell Science (NCCS), Pune, India. Cell culture reagents including fetal bovine serum (FBS, #RM10685), MTT reagent (5 mg/mL, #4060), and Dulbecco's phosphate-buffered saline (D-PBS, #TL1006) were procured from Himedia [4].

Reagents and Chemicals

Analytical grade carbohydrates—sucrose, glucose, and fructose—were utilized for nanoparticle synthesis. Standard chemotherapeutics camptothecin (#C9911, Sigma) and oxaliplatin (#O9512, Sigma) were employed as reference drugs for HepG2 and MCF-7 assays, respectively.

Synthesis of Carbon Dot Nanoparticles (C-Dots)

Carbon dots were generated via an acidic oxidation method using individual carbohydrate precursors. Briefly, 0.698 g of sucrose, 0.1396 g of glucose, and 0.1396 g of fructose were each dissolved in 150 mL of distilled water in separate beakers. To each solution, 0.106 mL of phosphoric acid (H_3PO_4) was added, and the mixtures were heated at 60°C on a mantle until a pale yellow coloration, indicative of C-dot formation, appeared (Figure 1). The resulting solutions were subsequently dialyzed for 24 hours using dialysis tubing to remove unreacted molecules and by-products. Detailed characterization and synthesis methodology were previously reported [4,5].

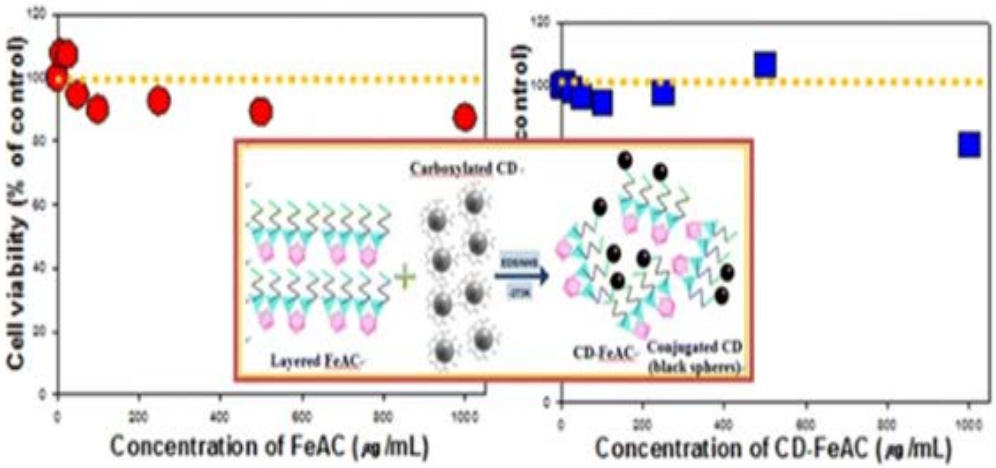

Figure 1: Variation in cytotoxicity of Carbon Dot nanoparticles (FCD, GCD, SCD) against HepG2 cells at different concentrations, showing percentage cell viability.

Maintenance of Cell Lines

HepG2 and MCF-7 cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% FBS, 1% penicillin-streptomycin solution, and maintained at 37°C in a humidified incubator with 5% CO_2. Cultures were allowed to reach confluency prior to their use in cytotoxicity assays.

Evaluation of Cytotoxicity Using MTT Assay

The cytotoxic potential of the synthesized C-dots derived from sucrose (SCD), glucose (GCD), and fructose (FCD) was assessed against HepG2 and MCF-7 cell lines using the MTT colorimetric assay. This method relies on mitochondrial dehydrogenases in metabolically active cells to reduce the yellow tetrazolium dye (MTT) into insoluble purple formazan crystals. The formazan was solubilized in DMSO, and absorbance was recorded at 570 nm to estimate cell viability.

For the assay, 200 µL of cell suspension containing approximately 20,000 cells per well was seeded into 96-well plates and allowed to attach for 12 hours. Various concentrations of C-dots (50, 150, 250, 350, and 450 µg/mL) were then applied to the wells, and the plates were incubated for 24 hours at 37°C with 5% CO_2. Following treatment, culture medium was removed, and 0.5 mg/mL MTT solution was added to each well. Plates were incubated for an additional 3 hours, after which the MTT solution was removed, and 100 µL of DMSO was added to dissolve the formazan crystals. Absorbance was measured using an ELISA plate reader at 570 nm [6-11].

The absorbance of untreated control wells was subtracted from treated wells to calculate net cell viability. Percent viability was determined using the following formula:

$$\%\text{Viability} = \left(\frac{\text{Absorbance of treated cells}}{\text{Absorbance of control cells}}\right) \times 100$$

Determination of IC_{50} Values

All experiments were performed in duplicate with two replicates for each concentration. The half-maximal inhibitory concentration (IC_{50}), representing the concentration of C-dots that reduced cell viability by 50%, was calculated from concentration–response curves using linear regression analysis (y = mx + c), where y = 50 (50% cell viability), and m and c were derived from the fitted line. This quantitative evaluation allowed comparison of the cytotoxic potency of C-dots synthesized from different carbohydrate precursors.

RESULTS

Cytotoxic Effects of Carbon Dot Nanoparticles

The cytotoxic potential of carbon dot nanoparticles synthesized from sucrose (SCD), glucose (GCD), and fructose (FCD) was evaluated against human liver carcinoma (HepG2) and breast adenocarcinoma (MCF-7) cell lines using the MTT assay (Figure 2). Initial viability assessments confirmed that all C-dot formulations maintained high cell survival (~90.85%) at baseline, indicating that the nanoparticles were suitable for subsequent cytotoxicity testing.

HepG2 Cell Line Cytotoxicity

Dose-dependent effects of the C-dot nanoparticles were observed on HepG2 cells. The half-maximal inhibitory concentration (IC_{50}) values were determined as 67.24 µg/mL for SCD, and less than 50 µg/mL for both GCD and FCD. The data showed that glucose-

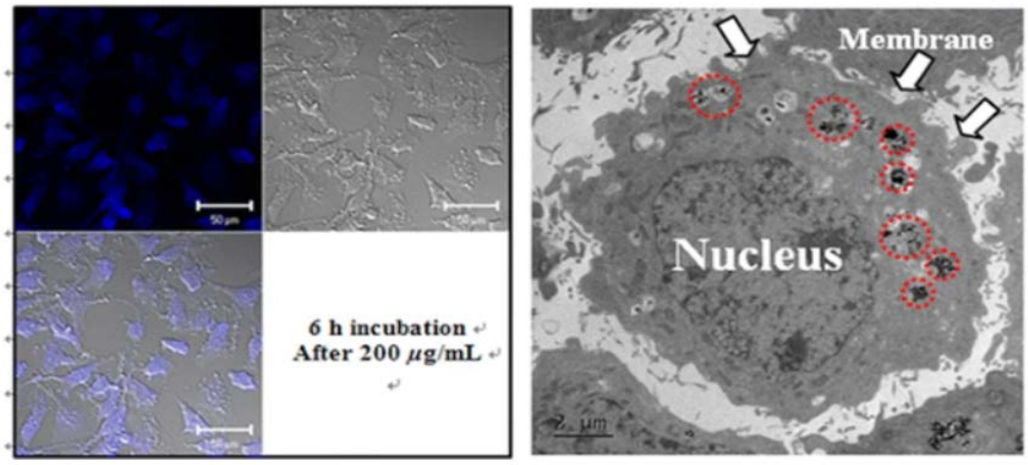

Figure 2: Effect of varying concentrations of Carbon Dot nanoparticles (FCD, GCD, SCD) on MCF-7 cell viability, indicating IC50 values for each formulation.

and fructose-derived C-dots exhibited stronger cytotoxic effects compared to sucrose-derived nanoparticles. A clear trend was observed where higher concentrations of C-dots resulted in reduced cell viability, while lower concentrations preserved a higher percentage of viable cells [12]. These findings indicate that the synthesized C-dots possess measurable anticancer activity against liver carcinoma cells, likely mediated by interactions with cellular metabolic or mitochondrial pathways.

Table 1: Cytotoxic effects of Carbon Dot nanoparticles (SCD, GCD, FCD) on HepG2 and MCF-7 cell lines. Percentage cell viability is shown at different nanoparticle concentrations (µg/mL), and IC50 values indicate the concentration required to inhibit 50% of cell growth.

C-Dot Type	Cell Line	Concentration (µg/mL)	% Cell Viability	IC50 (µg/mL)
SCD (Sucrose)	HepG2	50	78.5	67.24
		150	62.3	
		250	54.8	
		350	46.7	
		450	38.2	
SCD (Sucrose)	MCF-7	50	88.1	105
		150	72.6	
		250	60.5	
		350	48.9	
		450	39.4	
GCD (Glucose)	HepG2	50	65.2	<50
		150	48.5	
		250	39.7	
		350	30.2	
		450	25.4	
GCD (Glucose)	MCF-7	50	60.5	<50
		150	42.8	
		250	34.9	
		350	28.7	
		450	22.3	
FCD (Fructose)	HepG2	50	62.4	<50
		150	46.7	
		250	38.5	
		350	32.1	
		450	26.9	
FCD (Fructose)	MCF-7	50	58.3	<50
		150	44.1	
		250	36.8	
		350	29.5	
		450	24.7	

Notes:

- % Cell viability decreases with increasing C-dot concentration.
- IC50 values indicate the concentration required to inhibit 50% of cell growth.
- HepG2 = human liver carcinoma cells; MCF-7 = human breast carcinoma cells.

MCF-7 Cell Line Cytotoxicity

A similar pattern was noted in MCF-7 cells. The IC_{50} values were 105 µg/mL for SCD, and less than 50 µg/mL for both GCD and FCD. The cytotoxicity profiles demonstrated that fructose- and glucose-derived C-dots were more effective in reducing breast cancer cell viability compared to sucrose-derived nanoparticles [13] (Table 1). Percentage cell viability decreased with increasing nanoparticle concentrations, confirming a concentration-dependent cytotoxic response.

DISCUSSION

The results suggest that the carbon dot nanoparticles exhibit potent anticancer properties against both HepG2 and MCF-7 cells, with glucose- and fructose-derived C-dots showing superior activity. These findings are consistent with prior reports highlighting the ability of carbon-based nanomaterials to induce selective cytotoxicity in cancer cells while maintaining biocompatibility with normal cells. The enhanced activity of GCD and FCD may be attributed to differences in surface functional groups, particle size distribution, or cellular uptake efficiency compared to SCD.

Furthermore, the observed concentration-dependent cytotoxicity aligns with the mechanism of MTT assay, which measures mitochondrial enzyme activity. As the C-dot concentration increased, cellular metabolic activity decreased, reflecting reduced proliferation and enhanced cell death. These properties suggest that carbon dot nanoparticles have the potential to serve as effective nanotherapeutic agents with lower systemic toxicity than conventional metallic nanoparticles [14]. Carbon dots synthesized from simple sugars can act as promising candidates for anticancer applications, providing a foundation for future research into their mechanistic pathways and potential clinical translation.

CONCLUSION

In this study, carbon dot nanoparticles were successfully synthesized using a simple, cost-effective, and environmentally friendly wet chemical approach. The method demonstrates advantages in terms of ease of preparation, low production costs, and minimal ecological impact, making it suitable for diverse biomedical applications. The synthesized C-dots exhibited intrinsic biocompatibility and low toxicity, both in vitro and in potential in vivo contexts, highlighting their suitability for medical and pharmaceutical use. Cytotoxicity evaluations against human liver carcinoma (HepG2) and breast adenocarcinoma (MCF-7) cell lines revealed that these carbon dots possess significant

anticancer activity, with glucose- and fructose-derived C-dots showing particularly strong effects. These findings suggest that C-dots can serve as promising candidates for targeted anticancer therapies while minimizing the side effects associated with traditional metallic nanoparticles. The study underscores the untapped potential of carbon dot nanoparticles in drug development and encourages further research to explore their mechanistic actions, optimize their pharmacological properties, and expand their applications in anticancer drug discovery and nanomedicine.

CONFLICTS OF INTEREST

There are no conflicts of interest among the authors.

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