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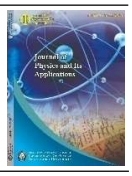

# Carboxymethyl Cellulose-Stabilized Platinum Nanoparticles Synthesized by Pulsed Laser Ablation for Enhanced CT Scan Contrast

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ABSTRACT

This study demonstrates the performance of platinum nanoparticles (Pt NPs) as contrast agents for computed tomography (CT). Synthesized through pulsed laser ablation, Pt NPs were stabilized in carboxymethyl cellulose (CMC). In CT imaging evaluations, the CMC-stabilized Pt NPs generated significantly higher Hounsfield Unit (HU) values and contrast-to-noise ratio (CNR) than both their counterparts and a conventional iodine-based agent. Remarkably, this enhanced contrast was achieved at substantially lower ppm concentrations, highlighting the potential of CMC-stabilized Pt NPs to offer a more efficient and powerful alternative to current clinical standards.

## 1. Introduction

Computed Tomography (CT) is a pivotal imaging technique in modern medicine, widely recognized for its excellent spatial resolution and cost-effectiveness. Despite these strengths, a fundamental challenge persists in its limited ability to distinguish between different soft tissues due to their similar X-ray attenuation properties [1,2]. To address this diagnostic shortcoming, contrast agents are employed as essential tools to enhance radiographic visibility. These agents function by increasing the differential absorption of X-rays, thereby improving the delineation between healthy and diseased areas and providing clinicians with critical diagnostic information [3,4]. For decades, iodine-based compounds have been the clinical standard, sanctioned by regulatory bodies worldwide. However, this established option carries significant limitations, including a relatively low sensitivity that necessitates the administration of high doses [5]. This practice can lead to adverse effects, from allergic reactions to diminished contrast efficacy, ultimately constraining the diagnostic quality of the images [6].

The emergence of nanotechnology has opened new frontiers in biomedical imaging, with metal-based nanoparticles presenting a compelling alternative to conventional agents [7]. Heavy metal nanoparticles, in particular, offer advantageous properties for CT imaging. They exhibit superior X-ray attenuation power, favorable physiological compatibility, and longer circulation times within the body compared to iodine [8]. These attributes translate directly into tangible benefits: the potential for enhanced image contrast, a reduction in the required injection dose, and a prolonged window for diagnostic imaging [9,10]. Consequently, the development of heavy metal nanoparticles as next-generation contrast agents is a highly promising research direction.

Platinum stands out as a candidate in this field. As a heavy metal with a high atomic number, it possesses an innate capacity for strong X-ray absorption [11]. Coupled with its renowned chemical stability and biocompatibility, platinum nanoparticles (Pt NPs) offer a powerful and safe platform for contrast enhancement [12]. Their high surface-to-mass ratio allows for biomedical applications. Among the various synthesis methods, pulsed laser ablation (PLA) in a liquid medium is a superior technique for producing such nanomaterials. This approach is straightforward, cost-efficient, and environmentally benign, as it requires no additional chemical precursors [13]. The process involves irradiating a solid platinum target submerged in a liquid with a focused laser beam, resulting in the direct generation of high-purity nanoparticles. A key advantage of PLA is the exceptional control it provides over critical nanoparticle characteristics, including size, distribution, and morphology [14,15].

This study investigates the synthesis of platinum nanoparticles using pulsed laser ablation within two different media: deionized water and a carboxymethyl cellulose (CMC) solution. The use of CMC, a biocompatible polymer, acts as a stabilizing surfactant designed to control nanoparticle growth and prevent agglomeration, thereby promoting better colloidal stability compared to a pure aqueous medium. Their performance was subsequently evaluated in vitro as an effective contrast agent for CT scanning.

Previous studies have established the potential of platinum in CT imaging, reporting on nanoparticles produced through methods like laser ablation of

alloys or sonochemical synthesis. While these have demonstrated promising Hounsfield Unit values, methods reliant on chemical synthesis often introduce impurities that can compromise nanoparticle quality and necessitate complex purification steps. Our work builds upon this a clean, chemical-free PLA synthesis to produce pure platinum nanoparticles. It specifically explores the role of a CMC matrix in enhancing nanoparticle characteristics for stability and performance, aiming to develop a highly effective and reliable alternative contrast agent.

## 2. Methods

A high-purity platinum plate (99.95%) was sterilized with 96% alcohol and thoroughly rinsed with distilled water prior to use. The plate was then submerged in 10 mL of liquid medium, either deionized water (DIW) or a 0.2% CMC solution. The CMC solution was prepared by dissolving 0.2 g of CMC powder in 100 mL of DIW under magnetic stirring for 60 minutes to achieve a homogeneous mixture.

Pt NPs were synthesized via pulsed laser ablation using an Nd:YAG laser (1064 nm wavelength, 80 mJ energy, 10 Hz frequency). The laser beam was focused to a spot size of approximately 50 μm onto a platinum target immersed in the liquid medium, resulting in an energy fluence of ~8 GW/cm$^2$. The ablation process was conducted for a duration of 3 hours per sample. During ablation, the beaker was slowly moved to promote homogeneous nanoparticle formation. The process involved plasma generation at the metal surface, leading to the ejection and dispersion of nanoparticles into the surrounding liquid. A schematic of the setup is provided in Fig. 1.

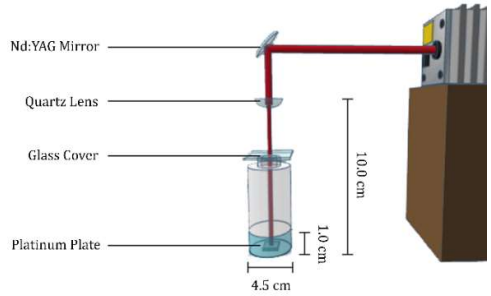


**Fig. 1:** Schematic diagram of the pulsed laser ablation setup used for the synthesis of platinum nanoparticles..

The concentration of the as-synthesized colloids was determined by Atomic Absorption Spectroscopy, yielding 10 ppm for DIW and 7 ppm for CMC. To enable a direct comparison, the DIW colloid was diluted to 7 ppm. A 100 ppm iodine solution served as the control variable for comparison. All solutions were placed in phantom vials for CT-scanning (GE Medical System). A helical scan protocol was used with tube voltages of 80, 100, and 120 kV, while the tube current was constant at 200 mAs and slice thickness at 1.25 mm (Fig. 2). This setup was designed to evaluate the contrast performance of the lower-concentration Pt NPs against the standard iodine agent. The CT scanning was performed using a clinical CT scanner. A standardized helical scan protocol was employed with tube voltages of 80, 100, and 120 kV. The tube current was held constant at 200 mAs, and the scan was conducted with a slice thickness of 1.25 mm. The phantom vials containing the nanoparticle solutions and the iodine standard were positioned in the scanner isocentre to ensure consistent imaging geometry.

For the quantitative analysis, five consecutive slices from the central region of each vial were selected to avoid partial volume effects. These images were processed using the IndoQCT software. A circular Region of Interest (ROI) with a diameter of approximately 5 mm was manually placed at the center of the sample to obtain the mean Hounsfield Unit ($HU_{object}$) and its standard deviation. A separate ROI of identical size was placed on the surrounding water within the phantom to obtain the mean background attenuation ($HU_{background}$) and its standard deviation ($SD_{background}$). The linear attenuation coefficient (μ, in cm$^{-1}$) for each sample was subsequently calculated from the mean HU value using the established relationship:

$$\mu = (HU / 1000 + 1) * \mu_{water} \quad (1)$$

where $\mu_{water}$ is the linear attenuation coefficient of water at the respective tube voltage. This quantitative analysis allowed for a direct comparison of the fundamental X-ray attenuation properties of the materials.

**Fig. 2:** Sample setup for CT scanning, showing the vials with Pt NPs in DIW, Pt NPs in 0.2% CMC, iodine solution, and a DIW control.

## 3. Results and Discussion

The synthesized nanoparticle colloids were stored in a closed environment, and their visual appearance was documented after a six-week period. Figure 3(a) and 3(b) show the Pt NPs prepared in DIW and CMC immediately after synthesis and after six weeks in storage, respectively.

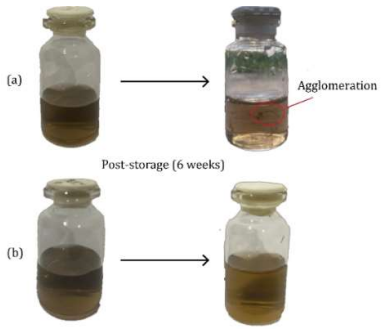


**Fig. 3:** (a) Platinum nanoparticles in DIW medium and (b) Platinum nanoparticles in 0.2% CMC medium.

The marked difference in colloidal stability between the two media, evidenced visually over a six-week period (Fig. 3), highlights the influence of the liquid environment on nanoparticle behavior post-synthesis. The aggregation and eventual sedimentation observed in the DIW-based colloid are a direct result of the absence of effective stabilizers. In this system, Pt NPs rely solely on a weak electrostatic double layer for stability [16]. Over time, this repulsive barrier is overcome by persistent Brownian motion and inherent van der Waals attraction, leading to irreversible agglomeration and precipitation as particle mass increases [17].

In contrast, the pronounced stability of the colloid synthesized in the 0.2% CMC medium is explained by two primary mechanisms: viscosity-modulated kinetics and steric stabilization [18]. The increase in viscosity by the CMC solution directly influences particle dynamics by increasing the resistance within the fluid medium. This dampens the Brownian motion of the nanoparticles, thereby reducing both the frequency and the kinetic energy of interparticle collisions. This suppression of particle mobility decelerates the diffusion-limited aggregation process that otherwise leads to agglomeration.

The more dominant mechanism involves CMC functioning as a steric stabilizer [19]. The polymer chains adsorb onto the surfaces of the Pt NPs, forming a protective hydrophilic layer. This adsorbed polymer layer creates a physical barrier that prevents the nanoparticles from approaching sufficiently close for short-range attractive forces to become significant. The stabilization is further enhanced by entropic repulsion forces that arise when the polymer layers are compressed during a close encounter [20]. Additionally, the anionic carboxymethyl groups on the polymer can impart a weak negative charge, contributing an electrostatic repulsive force [21]. This combination results in an electrosteric stabilization mechanism. This dual-action mechanism is more effective than stability from electrostatic forces alone, effectively protecting the nanoparticles and ensuring the long-term colloidal stability required for biomedical and other applications.

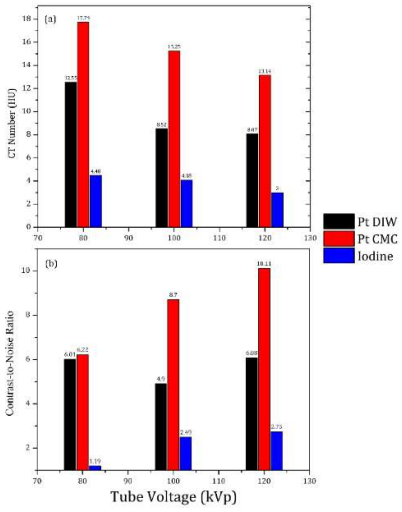


**Fig. 4:** Comparison of (a) CT number and (b) CNR values between platinum nanoparticles (Pt NPs) in DIW medium, 0.2% CMC medium, and iodine contrast agent at tube voltages of 80 kV, 100 kV, and 120 kV

The X-ray attenuation performance of the synthesized Pt NPs was evaluated against a commercial iodine agent, with the results for CT number and CNR detailed in Figure 4(a) and 4(b), respectively.

A consistent inverse relationship between tube voltage and HU value was observed for all contrast agents, as shown in Figure 4(a). This phenomenon is characteristic of high-atomic-number (Z) materials like platinum (Z=78) and iodine (Z=53), where the photoelectric effect, the dominant interaction at lower energies, diminishes as the incident photon energy (kV) increases. The HU scale, which uses water as a reference standard, quantifies this differential attenuation, allowing for precise tissue density comparison in medical imaging.

The CNR analysis, which critically assesses the discernibility of the contrast agent from its background, revealed distinct performance profiles. The Pt NPs in DIW exhibited fluctuating CNR values, a pattern indicative of colloidal instability that impairs consistent X-ray interaction across different energy levels. In stark contrast, the Pt NPs stabilized in the 0.2% CMC medium demonstrated a robust, positive correlation between CNR and tube voltage, with values escalating from 6.22 at 80 kV to 10.11 at 120 kV. This sustained enhancement underscores the role of CMC in providing superior dispersion and stability, which translates to more reliable and effective contrast. Meanwhile, the iodine agent, while showing a slight increase in CNR with voltage, was significantly outperformed by both Pt NP formulations at every voltage setting, despite being tested at a higher concentration.

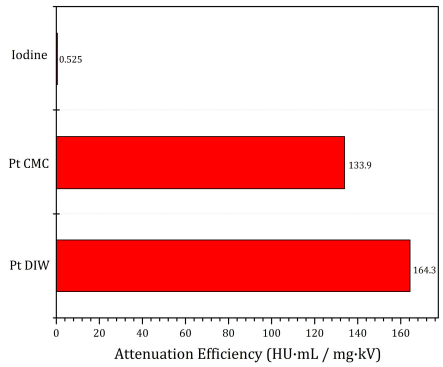


**Fig. 5:** Calculated X-ray Attenuation Efficiency

The X-ray attenuation performance was further quantified by calculating the attenuation efficiency using Eq. (1), which normalizes the measured Hounsfield Units (HU) by the mass concentration and tube voltage similar to a previous study [22]. This parameter provides a direct comparison of the attenuation power of the contrast agents, independent of concentration and scanning energy. As depicted in Fig. 5, the platinum nanoparticles exhibited a higher attenuation efficiency compared to the iodine standard. For instance, at 80 kV, the efficiency of the Pt NPs in CMC (164.3 HU·mL/mg·kV)

was over 300 times greater than that of iodine (0.525 HU·mL/mg·kV). This difference underscores the superior X-ray attenuation capabilities of platinum, attributable to its higher atomic number and density, and highlights the potential for achieving high contrast at drastically reduced metal concentrations.

## 4. Conclusion

In summary, this study successfully demonstrates the synthesis of Pt NPs via pulsed laser ablation in both DIW and a 0.2% CMC solution. When evaluated for computed tomography, the Pt NP colloids consistently generated superior HU and CNR values compared to a conventional iodine-based contrast agent. The most significant enhancement was observed with the CMC-stabilized nanoparticles. The 0.2% CMC matrix proved highly effective in promoting nanoparticle stability and dispersion, which directly contributed to its exceptional performance across all tested tube voltages. Consequently, these findings demonstrate that platinum nanoparticles synthesized in a 0.2% CMC medium exhibit significant potential as a candidate for future contrast agents in advanced CT imaging applications. Future work will focus on essential evaluations of their long-term biocompatibility and in vivo efficacy, including validation in biological tissue phantoms and animal models.

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