Ultrasound-mediated Gold Nanoparticles Delivery in Human Breast Cancer Cells

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1. Introduction

In recent years, significant advancements have been made in cancer treatment modalities, including surgery, chemotherapy, radiation therapy, and immunotherapy. Especially breast is a most common diagnosed cancer among females [1]. Nonetheless, the administration of chemotherapeutic drugs can lead to drug resistance and raise the risk of cancer recurrence [2]. Moreover, the limited accumulation of drugs within cancer cells can compromise the efficacy of breast cancer treatments [3, 4]. The efficiency of treating various ailments heavily depends on targeted drug delivery [5]. Ultrasound emerges as a promising avenue, offering non-invasiveness and remarkable tissue penetration. It presents itself as a viable solution to address the drawbacks and limitations associated with conventional techniques. A groundbreaking investigation, conducted by Umemura et al. in 1989, represented a significant advancement in the field by showcasing that ultrasound can generate reactive oxygen species capable of eliminating cancer cells. Since then, numerous research efforts have been dedicated to unraveling the mechanisms and exploring the potential applications of ultrasound in cancer therapy. Ultrasound has demonstrated particular effectiveness in facilitating the delivery of nanoparticles for cancer treatment.

2. Materials and Methods

2.1 Cell Culture

Human breast cell lines MCF-7, obtained from Korean Cell Line Bank, were cultured in RPMI-1640 medium. The density of 5×10^4 MCF-7 cells were seeded in cell dish. These cells were grown at 37 ℃ in the incubator containing 5% CO_2.

2.2 Gold Nanoparticles

A diameter of 50 nm gold nanoparticles (GNPs) and the concentrations of GNPs for cells were 20 μg/ml (Sigma-Aldrich Co., USA). Cells were incubated with GNPs for 3 h before ultrasound irradiation.

2.3 Ultrasound Irradiation System

The ultrasound irradiation system used an ultrasound transducer (Vurch Co., Seoul, Korea) frequency of 40 kHz. The transducer was submerged in the cell culture medium. Ultrasound irradiation durations of 5, 10, and 20 min were applied to the cells. Following irradiation, cells were fixed at three different time points: immediately (0 h), after a 3 h interval, and after 24 h.

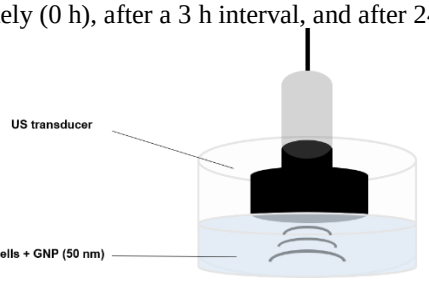

Fig. 1. Ultrasound immersion exposure system in MCF-7 cell medium

2.4 GNP Quantification through ICP-AES

Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES) (OPTIMA 8300, USA) was used for intracellular GNP quantification. The equation relates particle mass concentration to average particle number [6].

$$N_{Au1} = \frac{C_{Au}}{\frac{4}{3}\pi\rho_{Au}\left(\frac{d}{2}\right)^3 N_c} \cdot V_{Au}$$

Where N_{Au1} represents the particle number, C_{Au} is the GNPs concentration, ρ_{Au} is gold density, d is the diameter of GNP, N_C is the total cell number, and V_{Au} is the original GNP volume,.

3. Results and Discussion

3.1 Post-ultrasound Exposure Time dependent Intracellular GNPs Quantification with ICP-AES

The mean count of intracellular gold nanoparticles (GNPs) at 0 hours following ultrasound exposure varied under 10,000, depending on the duration of ultrasound

irradiation. However, after 3 h of ultrasound exposure, there was a decline in the average count of intracellular GNPs. It was noted that the increase in GNP count did not directly correlate with the duration of ultrasound irradiation. Nevertheless, ultrasound irradiation for 5 and 20 min immediately after exposure initiation was observed to enhance the count of intracellular GNPs. Additionally, ultrasound exposure for 10 and 20 min at 24 h post-exposure resulted in an augmentation of GNP delivery.

ICP-AES

Cell samples	0 h (10^2 part)	3 h (10^3 part)	24 h (10^3 part)
MCF-7 (0 min ultrasound)	20.51	12.19	16.29
MCF-7 (5 min ultrasound)	28.27	10.19	14.35
MCF-7 (10 min ultrasound)	16.38	10.24	17.79
MCF-7 (20 min ultrasound)	72.42	10.79	18.29

Table. 1. Average GNP numbers per cell at each post-ultrasound exposure time.

4. Conclusions

Our study has demonstrated that utilizing low-frequency ultrasound effectively enhances the delivery of GNPs into MCF-7 cancer cells, as evidenced by quantifying cellular uptake. The relationships between GNP uptake, ultrasound irradiation duration, and post-ultrasound exposure periods appeared unclear within our experimental framework. Nevertheless, employing low-frequency ultrasound immediately after irradiation emerges as a promising strategy to enhance nanoparticle delivery into cancer cells. Moreover, prolonging the time interval following ultrasound exposure revealed a predominance of intrinsic uptake mechanisms over ultrasound-induced sonoporation effects. By supplementing this approach with optimized ultrasound parameters, we anticipate achieving efficient and targeted delivery, potentially mitigating the adverse effects commonly associated with conventional cancer treatments.

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