# Ultrasound-mediated Drug Delivery with Drug Screening

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## 1. Introduction

Cancer remains a significant global health threat. Various treatment modalities, such as surgery, radiation therapy, and chemotherapy, have been developed to combat cancer cells. Especially for worldwide woman, breast cancer take one of the highest diagnosis rate and is hard to treat. However, chemotherapeutic drugs can lead to drug resistance and face limitations in local delivery to the target site [1, 2]. Ultrasound has emerged as a selective method to enhance cancer treatment efficacy [3]. The cavitation effect of ultrasound generates microbubbles through changes in liquid velocity and pressure. These microbubbles enhance sonoporation, which involves the creation of pores in the cell membrane. This phenomenon facilitates the internalization of drugs or nanoparticles. Cellular uptake of nanoparticles is crucial for determining the efficacy of cancer cell treatment. To isolate the effect of ultrasound on cells, it is essential to maximize cell numbers and minimize the cytotoxic effects of drugs. Therefore, drug screening is a critical aspect of ultrasound experiments. In this study, drug screening was conducted to assess the impact of ultrasound alone on cells.

## 2. Methods and Results

### *2.1 Cell Culture and nanoparticles*

Human breast cancer, lung adenocarcinoma, and ovarian cancer cell lines were cultured in a growth medium at 37°C in an incubator with 5% $CO_2$. Five types of nanoparticles were injected into each cell line at various dilutions.

Table 1: Cell line and nanoparticle type

| Nanoparticle | | Cell line | | | |
|---|---|---|---|---|---|
| Name | Diameter | | | | |
| Sigma GNP | 50 nm | MCF-7 | | | |
| IMP301 | 130 nm | MCF-7 | | | |
| Bare GNP | 40 nm | MCF-7 | MDA-MB-231 | A549 | SKOV3 |
| GNP wt | 67 nm | MCF-7 | | MDA-MB-231 | |
| GNP wt PEG | 158 nm | MCF-7 | | MDA-MB-231 | |

### *2.2 Cell viability assay*

After 24 h of drug treatment, cell counting kit-8 was used for cell viability assay. (N=3)

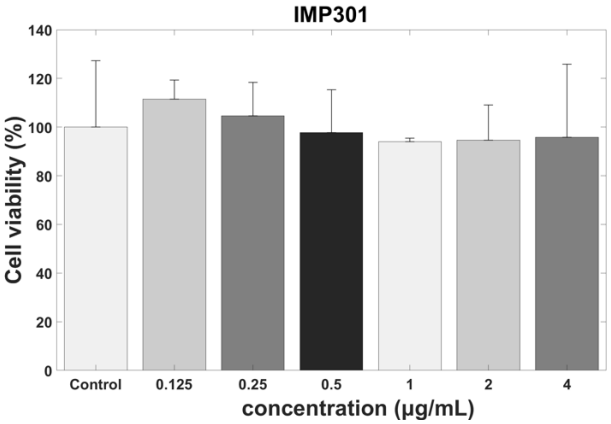


Fig. 1. MCF-7 breast cancer cell viability with IMP301.

### *2.3 Ultrasound irradiation*

The frequency of 40 kHz ultrasound transducer was submerged in the cell medium for irradiation. Cells were exposed to ultrasound for duration of 5, 10, 20 min.

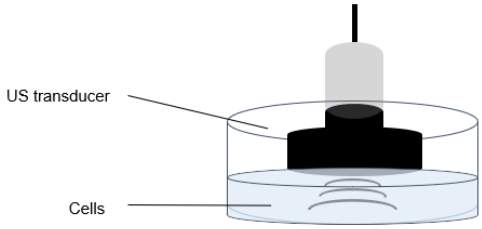


Fig. 2. Ultrasound exposure system for GNP with MCF-7 cell

*2.4 Nanoparticle quantification with ICP-AES*

Cell fixation was performed at three different time intervals: 0 h, 3 h, 24 h after ultrasound irradiation. The fixed cells were then analyzed using inductively coupled plasma atomic emission spectroscopy (ICP-AES), a gold standard method for nanoparticle quantification.

Table 2: ICP-AES results

| | **ICP-AES** | | |
|---|---|---|---|
| **US irradiation** | **0 h ($10^2$ particle)** | **3 h ($10^3$ particle)** | **24 h ($10^3$ particle)** |
| 0 min | 20.51 | 12.19 | 16.29 |
| 5 min | 28.27 | 10.19 | 14.35 |
| 10 min | 16.38 | 10.24 | 17.79 |
| 20 min | 72.42 | 10.79 | 18.29 |

## 3. Conclusions

Each nanoparticle and drug exhibited distinct cytotoxicity profiles. The drug screening results revealed that the maximum concentration of nanoparticles required to maintain over 80% cell viability is crucial. Notably, bare gold nanoparticles (GNPs) exhibited no cytotoxicity, and ultrasound was applied to cells using non-cytotoxic nanoparticle concentrations. An increase in concentration was observed in breast cancer cells, up to 3.5-fold. These findings highlight the necessity of drug screening in ultrasound experiments and demonstrate that ultrasound can enhance the internalization of nanoparticles into cells.

## REFERENCES

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