Gold Nanorods and Paclitaxel Loaded Solid Lipid Nanoparticles and Their Therapeutic Potential for Near-Infrared Photothermal-Chemotherapy of Cancer

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ABSTRACT SUMMARY
This study presents a new single particle drug delivery system for concurrent near-infrared (NIR) photothermal-chemotherapy of cancer. Paclitaxel (PTX) and cholesterol modified gold nanorods (GNR-chol) were successfully loaded into the core of solid lipid nanoparticles (SLNs). These nanoparticles were able to deliver high concentration of gold nanorods to cancer cells to absorb NIR laser strongly to create heat sufficiently to induce tumor ablation in conjunction with paclitaxel.

INTRODUCTION
Nanotechnology-based Photothermal therapy (PTT) has emerged as a promising treatment for cancer during the past decade.1 However, heterogeneous laser heating and limited light penetration can lead to incomplete tumor cell eradication. One of the most promising approaches to overcome these limitations is to combine PTT with chemotherapy. Combined PTT and chemotherapy has been shown to be more effective than the two treatments alone due to additive or synergistic effects.2

In this study, we developed a NIR-absorbing cholesterol modified gold nanorods (GNR-chol) and paclitaxel (PTX) incorporated SLNs and identified their potential for therapeutic system combining PTT with chemotherapy of cancer.

EXPERIMENTAL METHODS
Hydrophobic agents cholesterol modified gold nanorods (GNR-chol) and paclitaxel (PTX) were incorporated into SLNs (gtSLNs) using a modified solvent-emulsification methods.3 Prior to synthesis of nanoparticles, GNR was synthesis using seed-mediated growth method1 and then modified by self-assembly with cholesterol-SH to make hydrophobic GNR-chol. Prepared nanoparticles were characterized by zetasizer and TEM to identified size, shape, and incorporation of GNR-chol into SLNs. ICP-MS and HPLC were also conducted to identify incorporation of GNR-chol and PTX into SLNs, respectively. Identifications of therapeutic potential of prepared nanoparticles for PTT and chemotherapy were performed individually as followed: 1) To investigate the photothermal potential, we evaluated the amount of heat generation upon NIR laser irradiation onto nanoparticle solutions (808 nm, 6.25 W/cm2, for 3 min.). 2) To investigate the chemotherapy potential, we evaluated the paclitaxel induced cell cytotoxicity of head and neck cancer cells, A431, after treatment with nanoparticles.

RESULTS AND DISCUSSION
The GNR was synthesized and modified with cholesterol to produce NIR-absorbing hydrophobic GNR-chol soluble in chloroform (Diameter x Length: 10 nm x 40 nm) as shown in figure 1.
Figure 1. (A) Demonstration of the solubilization effect of GNR modification with chol-SH. (B) TEM image and (C) Absorption spectrum of GNR-chol.

These gold nanorods were incorporated into the hydrophobic lipid core of SLNs. SLNs encapsulated hydrophobic GNR-chol and (or) PTX successfully (Figure 2, Table 1).

Figure 2. Schematic illustration of gtSLNs. Inserted image was measured using TEM to determine the shape of nanoparticles and GNR-chol incorporation into SLNs.

Table 1. Physicochemical properties of prepared SLN formulations

<table>
<thead>
<tr>
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<th>GTS</th>
<th>NTS</th>
<th>tSLNs</th>
<th>gSLNs</th>
<th>TSLNs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zeta die (nm)</td>
<td>122.2 ± 0.3</td>
<td>133.5 ± 0.3</td>
<td>144.3 ± 1.4</td>
<td>108.4 ± 0.8</td>
<td>153.2 ± 1.2</td>
</tr>
<tr>
<td>PDI</td>
<td>0.419</td>
<td>0.220</td>
<td>0.625</td>
<td>0.809</td>
<td>0.689</td>
</tr>
<tr>
<td>% of PTX incorporation efficiency</td>
<td>95.2 ± 0.2</td>
<td>80.8 ± 0.6</td>
<td>83.8 ± 0.6</td>
<td>80.3 ± 0.8</td>
<td>85.9 ± 0.8</td>
</tr>
<tr>
<td>% of GNR-chol incorporation efficiency</td>
<td>95.2 ± 0.2</td>
<td>80.8 ± 0.6</td>
<td>83.8 ± 0.6</td>
<td>80.3 ± 0.8</td>
<td>85.9 ± 0.8</td>
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The temperature increase due to the surface plasmon resonance (SPR) effect of the GNR-chol leads to potential hyperthermic effect (Figure 3).

The PTX-loaded SLN formulations effectively reduced the viability of A431 cells with increased PTX concentration (Figure 4). All types of PTX-free SLNs were not effective for cells viabilities, while blank Taxol® formulation containing no PTX showed very significant cytotoxicity because of cremophor-EL.

Figure 4. In vitro cytotoxic effect of nanoparticles against A549 cells after incubation for 72 hours at various concentrations of PTX. The viability of cells treated with PTX-free SLNs, gSLNs, and a mixture of cremophor-EL/ethanol was shown at an equivalent PTX concentration of 20 μM.

CONCLUSION

We demonstrated that the gtSLNs did exhibit significant therapeutic potential for both PTT and chemotherapy. Through these results, combined PTT and chemotherapy using the gtSLNs will be demonstrated to be synergistic and highly effective, leading to complete cancer therapy in the future.

REFERENCES

ACKNOWLEDGMENTS

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