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Is Colloidal Gold with Camostat Mesylate Powder Strong Anti-Cancer Drug Enough?

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Abstract

Dosages of anticancer drugs are usually calculated on the basis of a uniform standard, the body surface area (BSA). Although many physiological functions are proportionate to BSA, colloid gold and camostat mesilate powder is only partially related to this parameter. A priori adaptive dosage determination, the relative contribution of identifiable drug therapy and disease state that influence plasma drug concentrations; dosage regimen is each patient's profile these characteristics. Although toxicity major anticancer drugs, this solution has no toxicity improving efficacy the dose-response relationship.

Keywords: ***Colloidal gold; Camostat mesylate powder; Lung adenocarcinoma; Xenograft mouse model; Dose-response relationship***

1. Introduction

Camostat mesylate, an oral serine protease inhibitor, is used to treat chronic pancreatitis and reflux esophagitis. The approved maximum is 200 mg 3 times daily; of 600 mg 4 times daily has not been used in previous clinical trials. Multiple administration of camostat mesylate 600mg q.i.d. was well-tolerated and no safety concerns were raised [1].

We fed seven time-dose of colloid gold with camostat powder solution to the xenograft lung cancer mice, the metastatic lung adenocarcinoma [2,3].

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Colloidal gold is sub-micron gold nanoparticles suspended in a solvent, water. 1) unaggregated and monodisperse with narrow size distributions 2) in the desired solvent 3) at high concentrations 4) a well-defined surface 5) long shelf life and in a condition 6) with low concentrations of residual chemicals from the manufacturing process. Gold nanoparticles can be purified from soluble impurities by washing with clean buffer solutions. If the purity of the colloid gold is consistent, the toxicity is minimalized. The nominal adult dosage for MesoGold is one tablespoon (15 mL) daily, the dosage must be determined for each individual.

Most adults find their optimum dosage will be between 1 and 4 tablespoons, take 6 to 8 tablespoons daily. To your optimum dosage, start with two tablespoons daily for one week, then double to 4 tablespoons for week. For children start with a dosage of one teaspoon (5 mL) for every 70 pounds of body weight and doubling the dosage after one week. A large dosage is not harmful [4].

2. Materials and Methods

2.1 Chemicals

Camostat mesylate (Foipan) powder was from Ilsung Pharmaceuticals (South Korea). Colloid gold (Mesogold) was from Colloidal Science Lab (Westampton, New Jersey, USA).

2.2 Cell culture and reagents

Murine Lewis lung carcinoma cells were from the American Type Culture Collection, cultured in RPMI1640 supplemented with 10% fetal bovine serum and 1% penicillin/streptomycin (Gibco) in humidified incubators at 37ºC with 5% CO2. The tumor cells, 10 passages, are grown to 70%-85% confluence before harvested. After 48 and 72 h incubation, 20 μL of MTT solution (5mg/ml) was added to the each well and incubated at 37°C for 4 h. The supernatant was removed and 100 μL of DMSO was added and absorbance of plates were read on an ELISA reader at a wavelength of 570 nm.

2.3 Mouse xenograft model

Athymic nude mice (nu/nu) obtained from National Cancer Institute were used in all human tumor xenograft therapeutic studies. Tumors were implanted and the size was measured periodically at specified times, and treatment when tumor size reached 80 mm^3 or larger. Tumor size and body weight were recorded. An inoculum of 3×10^5 LLC lung carcinoma cells was injected subcutaneously on the flank of C57BL/6 mice in 100 μL serum-free media. Four days after injection, the treatment was initiated per orally. The tumor volume was calculated as $0.5 \times \text{length} \times \text{width}^2$. The tumors were allowed to grow. This study was reviewed and approved by the Institution of Animal Care and Use Committee of Ewha Womans University (approval number: IACUC-21-005).

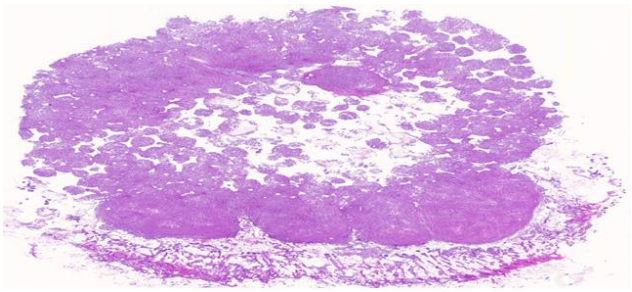
2.4 Caliper measurements of subcutaneous xenografts

Two longest perpendicular axes in the x/y plane of each tumor were measured to the nearest 0.1 mm. The depth was the shortest of the perpendicular axes. Measurements were made using a digital vernier caliper while mice were conscious and were calculated according to equation: Xenograft volume = $xy^2/2$.

3. Results

The tumor mass is well demarcated with the adjacent normal connective tissue, but poorly encapsulated. The neoplastic cells are forming cords or clusters, invading into the surrounding connective tissue. In addition, the neoplastic cells are forming atypical glandular structures or solid sheets in a wide range. The hyalinized fibrous strands are intervening between the neoplastic cell cords or clusters and glandular structures. Variable sizes of irregular cysts, lined by simple squamous epithelia, exist in the central area of the tumor. The neoplastic cells have eosinophilic cytoplasm and indistinct cellular boundaries with a high nuclear/cytoplasmic ratio. The nuclei of the tumor cells are vesicular and spherical or oval shapes with a prominent nucleolus. The nuclear size is variable and indicate pleomorphism. The mitotic figures are generally ranged 6~8 in number under a high-power field (FIG. 1 & 2). Nude mice bearing LLC lung carcinoma xenografts were treated orally beginning on day 1, after tumor implantation, with 500 µl of 10 cc colloidal gold and 100mg camostat mesylate powder solution daily. Transcriptional differences, the different growth ratios, and multiple genes are involved in these differences. In this study, saline served as a negative control. Treatment with the solution led to 50% suppression on day 10 (FIG. 3 & 4).

control



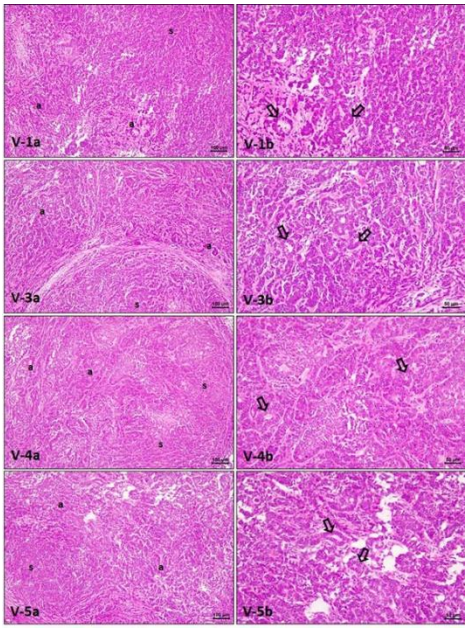
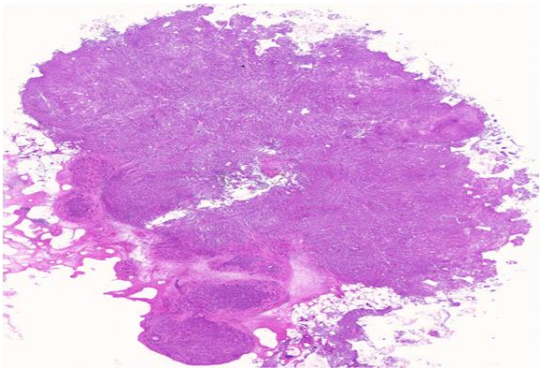


FIG. 1. **Histological features of the tumors of control group. In the lower power field (left 'a' figures), note the gland-like structures (acinar type area, a) and solid patterned areas (s); the glandular structures are magnified in the right 'b' figures (thick open arrows). H&E. Bars=100µm for 'a' figures, and 50 µm for 'b' figures.**

treatment group



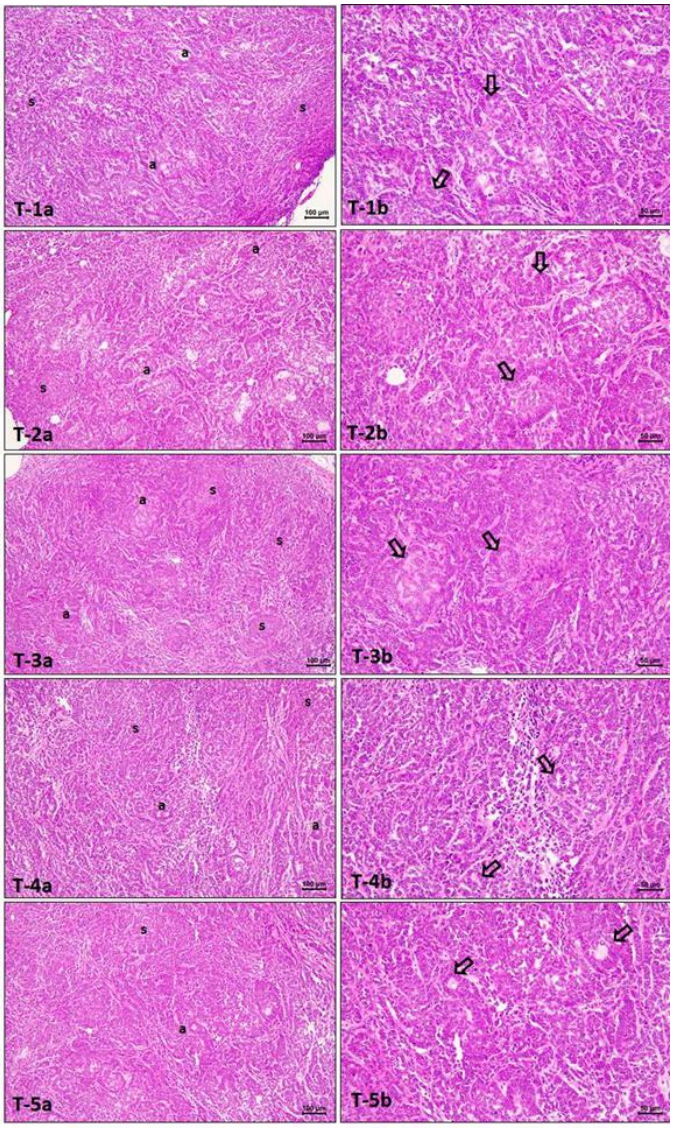


FIG. 2. **Histological features of the tumors of treatment group. In the lower power field (left 'a' figures), note the gland-like structures (acinar type area, a). The glandular structures are magnified in the right 'b' figures (thick open arrows). H&E. Bars=100µm for 'a' figures,and 50µm for 'b' figures.**

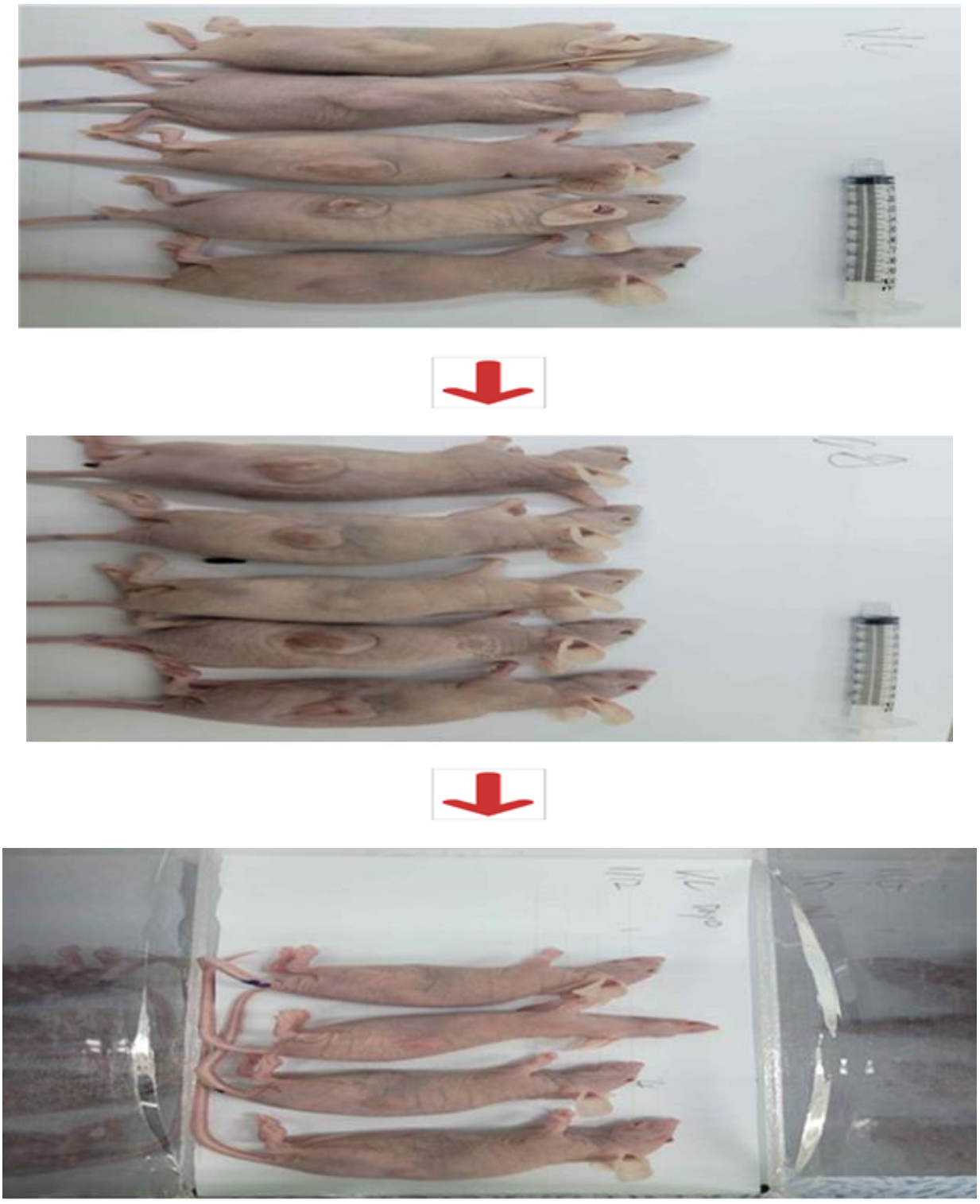


FIG 3. **Typical photos of mice with microscopic images on day 7, 14 and day 21 for the experiment shown in oral therapy of lung adenocarcinoma xenograft tumor with colloid gold + camostat mesilate powder.**

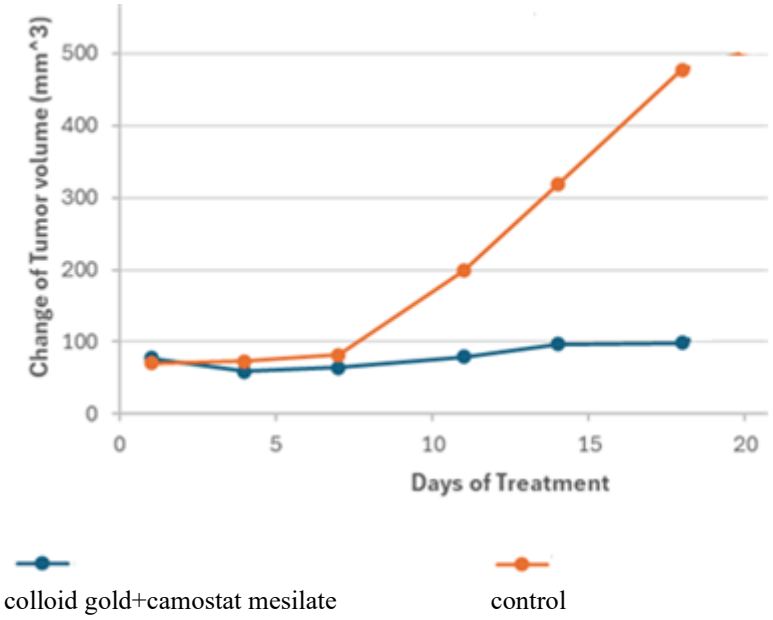


FIG 4. **80% tumor growth inhibition was shown at 18 days after implantation.**

4. Discussion

Gold-based therapeutic agents are used in human diseases: degenerative, infectious diseases and cancer, which combines high selectivity in targeting tumor cells and low toxicity. In mice treated with gold alone, the growth of tumor cells was not halted, suggesting a synergistic effect between gold and camostat mesilate. The potency of tumor size reduction by colloidal gold-based nanoparticles can be compared to the potency of paclitaxel to solid tumors [5]. Gold nanoparticles have been using on pancreatic cancer, colon cancer, squamous cell carcinoma of the hypopharynx, prostate cancer, breast cancer, lung cancer, hepatocellular carcinoma.

Camostat mesylate, an oral serine protease inhibitor, is used to treat chronic pancreatitis and reflux esophagitis, its active metabolite 4-(4-guanidinobenzoyloxy) phenylacetic acid (GBPA) to inhibit severe acute respiratory syndrome coronavirus 2 by inhibiting type II transmembrane serine protease. Camostat mesylate inhibits DNA methylation along with ACE2 gene methylation and post-translational histone modifications. The epigenetic regulation of gene expression relies on post-translational chemical changes that occur at the level of chromatin as well as on RNA and DNA, including primary methylation, acetylation, phosphorylation, ubiquitination and sumoylation. This bridges genotype and phenotype by altering function without changing the underlying DNA sequence.

5. Conclusion

At seven times dosage to the standard dose, colloid gold with camostat mesilate powder has more potent anti-cancer effect than that of the standard dose without showing any side effect.

6. Conflict of Interest

No conflict of interest.

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