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**Abstract:**

Strategy, Management and Health Policy Enabling Technology, Genomics, Proteomics Preclinical Research Preclinical Development Toxicology, Formulation Drug Delivery, Pharmacokinetics Clinical Development Phases I-III Regulatory, Quality, Manufacturing Postmarketing Phase IV This study assessed the in vivo antitumor efficacy of a polypeptide-based poly-L-glutamic acid-gemcitabine conjugate (PG-G). PG-G was synthesized by conjugating gemcitabine to poly-L-glutamic acid by a carbodiimide reaction. PG-G was evaluated for its in vivo antitumor efficacy and toxicity using 4T1 murine breast tumor-bearing mice. The antitumor effects of PG-G were superior to those of unconjugated gemcitabine in both single and four-consecutive dosing studies. Tumor regression was observed within 1 day after PG-G administration and continued for 45 days. Thereafter, tumors grew at a slower rate compared with the unconjugated gemcitabine treatment group and other control groups. The main toxicity observed from the Berlin test was an apparent reversible weight loss of 1012%. The unconjugated gemcitabine treatment group also demonstrated a similar, but reduced, weight loss trend. The present study demonstrates that the PG-G formulation exhibits a significant antitumor activity in the aspects of tumor growth inhibition and shrinkage that is more robust than the parent drug and other control groups. Thus, the PG-G dose regimen may be optimized to minimize side effects and render it a potential anticancer therapeutic.

**Keywords:**
cancer; drug delivery systems; polymeric drugs; prodrug; gemcitabine; poly-L-glutamic acid

**Suggested Citation:**

**Full text available here:**