# Examination of a Polyacrylate Hydrogel System for Extended Cisplatin Delivery

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**Introduction:** As a potent chemotherapeutic drug for different cancers, cisplatin has significant toxic side effects particularly after chronic administration **(1)**. Clinical administration of cisplatin is by intravenous infusion, but this route of administration is restricted by low cisplatin solubility, toxicity, and a short plasma half-life. Therefore, new methods of delivering cisplatin are needed to better treat various malignant diseases. By incorporated cisplatin into poly(acrylate) hydrogels, it was hypothesized that cisplatin complexation could be controlled to achieve extended delivery. The purpose of this study was to develop a polyacrylate hydrogel for cisplatin incorporation and to confirm cisplatin release profile.

**Methods:** Acrylic acid, poly(ethylene glycol) diacrylate (PEGDA), and ammonium persulfate (APS) were mixed with cisplatin (3.2 mg/mL) before polymerization. The monomer-cisplatin solution was polymerized at 37ºC for 4 hours in glass molds. The surface morphology of poly(acrylic acid) [p(AA)] hydrogels and cisplatin-p(AA) hydrogels before and after *in vitro* release were examined by scanning electron microscopy (SEM) and light microscopy. *In vitro* cisplatin release was observed in phosphate buffered saline (PBS) at room temperature. Cisplatin bioactivity was monitored using vital staining and a modified MTT assay with U-87 MG human glioma cells.

**Results/Discussion:** Hydrogels appeared colorless, clear, and transparent when no cisplatin was incorporated. Cisplatin-p(AA) hydrogel appeared slightly yellow, clear, and transparent indicating few macroscopic crystals present. The surface of p(AA) hydrogels was smooth under SEM examination while cisplatin crystals could be observed embedded in cisplatin-p(AA) hydrogels. After 30 days of release, cavities were observed on the surface of cisplatin-p(AA) hydrogel indicating that the crystals were probably not due to dehydration of the hydrogels. *In vitro* release of cisplatin from p(AA) hydrogel was extended up to 30 days with a burst release of forty percent of incorporated cisplatin during the first half day, Figure 1. About ninety percent of cisplatin was release at the end of thirty days.

Untreated glioma cells showed high viability and regular morphology. Glioma cells treated with cisplatin (3mg/mL cisplatin in PBS) showed a low viability and irregular morphology, as shown in Figure 2. Cells treated with p(AA) hydrogels (no cisplatin present) showed no significant difference from untreated cells. Glioma cells treated with cisplatin-p(AA) hydrogels showed very low viability and abnormal morphology. Supporting viability studies results in glioma cells were shown to have high viability when treated by p(AA) hydrogel and low viability (~10% of negative control) for cells treated by cisplatin-p(AA) hydrogels.

The complexation between cisplatin and poly(acrylic acid) has been shown to reduce toxicity and keep activity of cisplatin **(2)**. The complexation was strong enough to prolong the cisplatin release from p(AA) hydrogel by decomplexation **(3)**. The prolonged release suggests that complexation with functional groups can change the release profile of cisplatin from a delivery system.

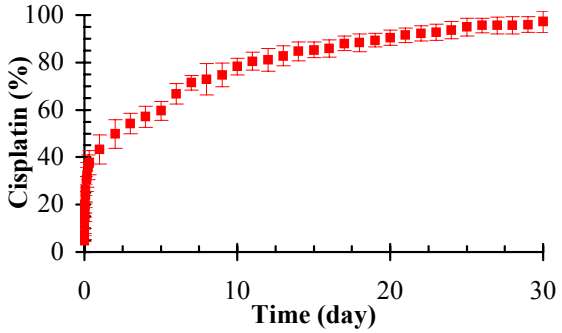


**Figure 1.** Prolonged release of cisplatin from p(AA) hydrogels due to complexation.

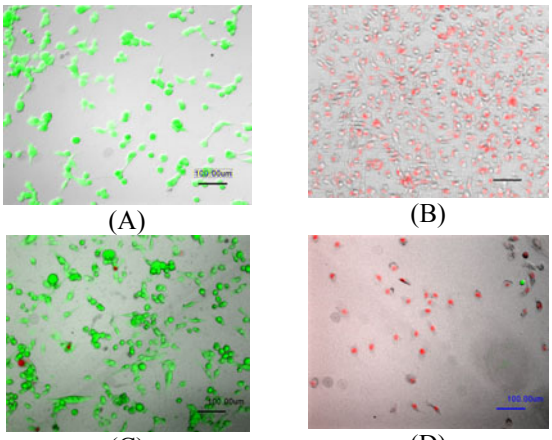


**Figure 2**. Live-dead assay after treatments of (A) PBS, (B) cisplatin, (C) p(AA) hydrogel, and (D) cisplatin loaded p(AA) hydrogel (scale bar = 100 μm).

**Conclusions:** A non-specific cisplatin delivery system was synthesized with the hope of creating systems for implantable cancer chemotherapy. The release of complexed cisplatin was prolonged and should have the ability to maintain cisplatin activity within the body for extended periods at levels suitable to inhibit tumor growth.

**References:** 1. Decatris MP. Cancer Treat. Rev. 2004;30:53-81. 2. Yan X. J. Control. Release. 2005;106:198-208. 3. Reedijk J. Proc. Natl. Acad. Sci. USA. 2003;100:3611-3616.

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