Development of Injectability Drug-Loaded SiC Particles for Intratumoral Treatment

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Introduction

Treating cancer with systemic drugs can cause severe side effects and low drug concentration at the tumor site. Localized drug delivery provides a targeted, less harmful alternative. Injectable bioactive ceramic materials, such as silicon carbide (SiC), are promising due to their ability to bind and release drugs while conforming to tumor shapes. Effective delivery requires the material to pass through a needle without clogging or high force. Ibuprofen may aid cancer treatment by inhibiting heat shock protein 70 (Hsp70), making cancer cells more susceptible to chemotherapy (Endo et al., 2014), and by reducing pro-inflammatory signals that support tumor growth (Shen et al., 2020). This project investigates how gel composition and particle loading affect injectability and drug release from ibuprofen-loaded SiC particles in alginate gels. Formulations were tested using a 16-gauge needle to measure injection force and flow rate, and samples were collected post-injection for drug release studies over 1–25 days.

Objectives

- Develop injectable gel-based formulations containing silicon carbide (SiC) particles loaded with ibuprofen salt
- Evaluate the force and flow rate required to inject the drug formulation through a 16-gauge needle
- Examine how gel concentration affects injection force and flow characteristics
- Collect injected formulations for drug release testing over a 1–25 day period
- Assess the potential of gel-based drug delivery systems for controlled, localized cancer treatment

Methods

Particle Preparation:

- SiC particles (90–150 µm and 150–250 µm) were immersed in 1.0096 g of ibuprofen salt mixed with 100 mL of DMSO for 48 hours, followed by drying in air at 37C for 12 hours. A fixed ceramic concentration of 20%was used in all gel mixtures.

Gel Formulation:

- Alginate gels were prepared at 2%, 2.5%, 3%, and 4% concentration by mixing specified volumes of alginate and deionized water (see Table 1 for exact ratios). One gram of drug-loaded SiC particles were incorporated into 5mL of each gel formulation.

Injectability Testing:

- Gel-particle mixtures were loaded into 5 mL syringes with 16-gauge needles and the injectability was tested using a 3D printed apparatus shown in Figure 2. A force was applied vertically onto the plunger of the syringe to initiate injection. The injection force and the corresponding ceramic suspension flow rate (µL/s) were recorded. Ideal flow range was defined as 100–200 µL/sec for intratumoral delivery.

Post-Injection Drug Release:

- The injected ceramic-gel mixtures were collected separately and each immersed in 10 ml PBS to determine drug release kinetics over 1–25 days.

Table 1: Composition of alginate gel with water volume and corresponding amount of alginate (by weight) used per gel concentration.

% Alginate	2%	2.5%	3%	4%
Water Volume (mL)	150	100	150	200
Alginate Weight (g)	3.0038	2.5003	4.5075	20.0448

Results and Discussion

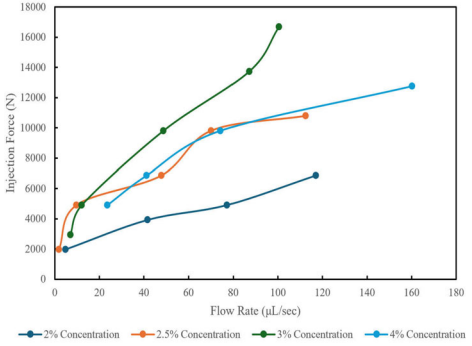

Figure 1: Force applied (N) and corresponding flow rate (µL/sec) recorded for each test weight. The legend identifies each gel concentration and its corresponding color-coded line representing the test data on the chart.

Figure 2: 3D printed testing apparatus. The loading weight was held by the circular plate and lifted to the peak of the device, then released to contact the plunger of the syringe. The syringe was held in place by the hollow, white cone, with the tip of the needle facing the base of the device. A container was placed in the hollow cone to catch the expelled gel from the syringe to later perform the drug release test.

Table 2: Data points from injectability tests showing the amount of force applied (N) and corresponding flow rate (µL/sec). The data is ordered by trial number, with increasing force, and concomitantly increasing flow rate, per test performed.

Gel Concentration	2%		2.5%		3%		4%	
	Force (N)	Flow Rate (µL/sec)	Force (N)	Flow Rate (µL/sec)	Force (N)	Flow Rate (µL/sec)	Force (N)	Flow Rate (µL/sec)
Trial 1	1962	4.8	1962	1.8	2943	6.96	4905	23.529
Trial 2	3924	41.7	4905	9.7	4905	12.03	6867	41.195
Trial 3	4905	77.2	6867	47.9	9810	48.78	9810	74.349
Trial 4	6867	117	9810	70.2	13734	87.21	12753	160.156
Trial 5	-	-	10791	112.5	16677	100.5	-	-

Injection Force Trends:

- Higher alginate concentrations required greater injection force.
- 3% and 4% gels exceeded 13,000 N at higher flow rates.
- 2% gels remained below 7,000 N and were easier to inject.

Flow Rate Observations:

- Flow rate increased with force across all concentrations.
- 4% gel achieved the highest flow (160 µL/sec) but needed high force (12,753N).
- 2% and 2.5% gels performed best within the ideal range (100–200 µL/sec).

Conclusions

The SiC-alginate mixture provided a successful system for injectable drug delivery system. Lower-concentration gels may offer better injectability for clinical use. Higher concentrations may improve stability but are harder to inject. At 20% (specify by volume or by weight??) ceramic concentration the 2% and 2.5% gels offered acceptable flow rate within the ideal range (100–200µL/sec).

Next Steps

- Drug release testing is ongoing and will continue over a 1–25 day period.
- Results will help evaluate how well each formulation performs for sustained, localized drug delivery.
- Test 5-Fluorouracil (5-FU) anticancer drug release kinetics.

References

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