NovaFlux PainGuard Implantable Hollow Fiber Constructs

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U-18, Translating Discoveries into Effective Devices to Treat Pain

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Motivation

In the U.S., around 3.6 million people live with amputated extremities, many facing persistent post-amputation pain. Existing treatments for this pain are limited, highlighting the need for innovative solutions. The current approach involves frequent hospital visits to apply anesthetic agents directly to injured nerves.

NovaFlux addresses this challenge with an implantable device delivering local anesthetics to injured nerves. The goal is to provide effective and long-term pain relief without the risk of systemic toxicity.

Hollow Fiber Implantable Devices

The drug is delivered directly to the nerve tissues from a hollow-fiber membrane fabric construct (Figure 1). The drug depot is loaded inside the lumens of the hollow fibers, which can diffuse through 5-10 nm pores. The hollow fiber ends are encased within two manifolds; each is connected to a micro-catheter so the device can be periodically refilled via a subcutaneous septum implanted under the skin. The device is designed to provide long-term drug therapy. The fabric (Figure 1a) is made with biocompatible polyamide-6 membrane hollow fibers woven within a polyester-supporting fabric. This soft fabric device is designed to wrap around the nerve to deliver the drug, thus allowing for radial inward diffusion into the nerve tissues during treatment (Figure 2). The hollow-fiber fabric has been developed and can be produced commercially.

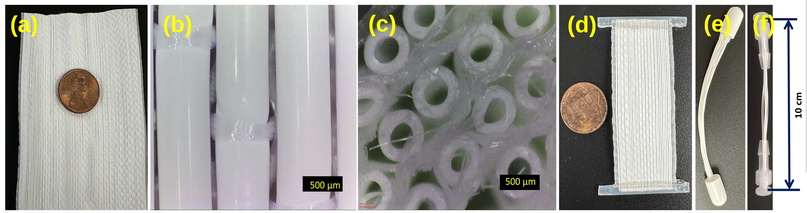

Figure 1: Hollow Fiber Fabric at Commercial Scale. (a) Hollow fiber fabric with an inner diameter of 300 µm and an outer diameter of 550 µm. Two different wall porosities are available: 5 nm or 10 nm. (b, c) Enlarged images providing a detailed view of the fiber fabric, with a cross-sectional structure shown; scale bar is 500 µm. (d) Constructs specifically designed for implantation around nerves. (e, f) Constructs composed solely of fibers, tailored for in-vitro studies.

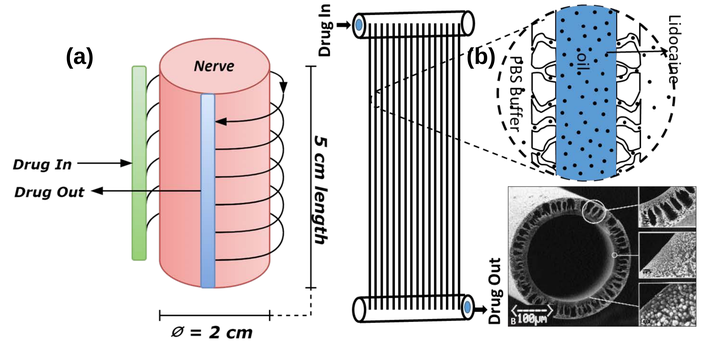

Figure 2: (a) Schematic representation of a nerve segment, encompassing about 10 mL of nerve tissue. The arrows and lines indicate the suggested arrangement of hollow fibers around the nerve, with arrows denoting the flow of the therapeutic formulation. (b) Illustration of a hollow fiber construct, featuring a cartoon representation of hollow fiber pores, along with a scanning electron microscope (SEM) image capturing a single hollow fiber.

In-vitro Drug Release – Protocol and Results

To assess the daily lidocaine release from the device, we used test constructs made of a small hollow fiber bundle with ends connected to a Luer fitting that connects to a syringe for loading with the drug formulation. During the test, the sealed test constructs (Figure 1f) are submersed in vials filled with phosphate-buffered saline (PBS), which are then immersed in a shaker water bath set at 37°C and 190 rpm. The released drug concentration was determined spectrophotometrically, and the vial, including the construct, was refilled with fresh PBS volume to continue monitoring the release kinetics. Figure 3 provides the test protocol.

The results indicate a supra-therapeutic release over a 7 – 30-day period for experimental constructs utilizing ten polyamide-6 fibers 10 cm long (refer to Figure 4 for graphical representations and Table 1.)

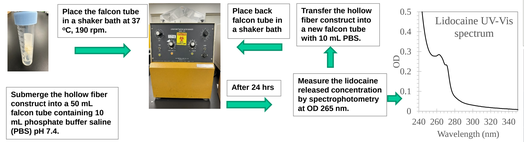

Figure 3. Experimental set of in-vitro lidocaine release kinetics

Table 1: An estimate of lidocaine release based on the number of fibers used in the construction of implantable devices.

No. of Fibers	Length	Inner Volume	Loading Capacity	Amount of Lidocaine Release at Day 10
1	10 cm	7 µL	4 to 6 mg	0.015 mg
10	10 cm	70µL	40 to 60 mg	0.15 mg
20	10 cm	140 µL	80 to 120 mg	0.30 mg
50	10 cm	350 µL	200 to 300 mg	0.75 mg

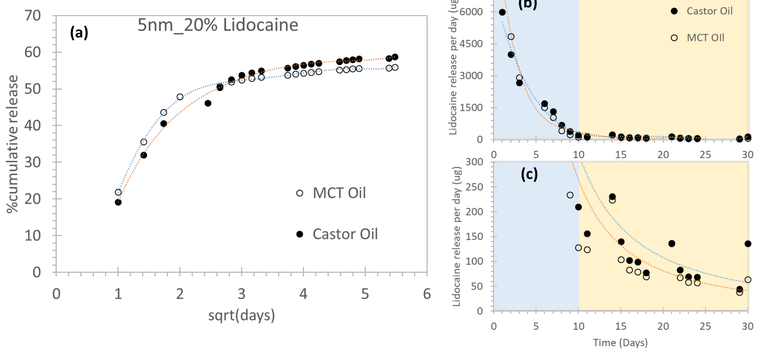

Figure 4: In an in-vitro experiment, lidocaine release kinetics are illustrated using a hollow fiber construct consisting of 10 fibers, each 10 cm in length, and featuring a pore size of 5 nm (see Figure 1f). The hollow fiber constructs were loaded with twenty percent lidocaine formulations, where open circles represent MCT oil formulations and filled circles represent castor oil formulations. (a) Depicts cumulative lidocaine release as a function of the square root of the number of days, while (b) and (c) show the amount of lidocaine released at different day intervals.

Highlights of NovaFlux PainGuard

The implantable hollow fiber construct for controlled drug delivery advantages:

- Wraps around the nerve, ensuring local-regional drug delivery into the nerve tissue.
- Can be periodically refilled (once per month) using a syringe with minimal supervision.
- Made from biocompatible implantable materials.

Novel lidocaine formulation has been developed for loading the device:

- High loading capacity of lidocaine, up to 30% (w/w)
- No effective osmotic stress caused by high drug loading
- No adverse pH effects, reducing the risk of irritation during local administration

The NovaFlux PainGuard technology allows tailoring of drug release for up to 30 days between refills. The estimated amount of drug released is expected to achieve an effective nerve-blocking action.

****Future investigations will focus on evaluating the pain-relieving effects of NovaFlux PainGuard in a rat model.****