Chemically Robust Microfluidic Devices for Radiochemistry Platforms

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ABSTRACT

We report the fabrication of solvent-compatible microfluidic devices based on Liquidia Technologies' Fluorocur™ materials. The materials are highly fluorinated functionalized perfluoropolyethers (PFPEs) that have liquid-like viscosities that can be cured into highly durable elastomers that exhibit the remarkable chemical resistance of fluoropolymers such as Teflon™. Unlike Teflon, these materials posses similar mechanical and optical properties to Poly(dimethylsiloxane) (PDMS). PDMS elastomers have become the material of choice for many recent microfluidic device applications. Despite the advantages of PDMS in relation to microfluidics technology, the material suffers from a serious drawback in that it swells in most organic solvents and reacts with acids, bases, and nucleophiles. Multilayer Fluorocur microfluidic devices containing air-actuated pneumatic valves were fabricated using multifunctional materials. Very strong adhesion capable of holding up to 60 psi without delamination was obtained. Device fabrication and valve actuation were accomplished using established procedures for PDMS devices. Fluorocur devices were used in the synthesis of radiolabelled biomarkers for positron emission tomography (PET) and compared to PDMS chips. Devices made from Fluorocur far outperformed device made from PDMS in terms of solvent and chemical compatibility. Microfluidic synthesis of PET biomarkers greatly reduces the synthesis time and volumes of material needed in traditional synthesis boxes.

Keywords: Microfluidics, Fluoropolymers, Microfabrication, PDMS, Positron Emission Tomography

1 INTRODUCTION

Poly(dimethylsiloxane) (PDMS) has rapidly become the material of choice for many microfluidic device applications.[1,2,3,4] PDMS offers numerous attractive properties in relation to microfluidics including low modulus, low surface energy, gas permeability, and ease of fabrication.[1,3] Despite the advantages of PDMS for microfluidics technology, this material suffers from a serious drawback in that it swells in most organic solvents.[4] Among those that greatly swell the material are hexanes, ethyl ether, toluene, dichloromethane, acetone, and acetonitrile.[4] Additionally, PDMS is reactive towards acids, bases, nuclephiles, and electrophiles making it incompatible with microchemistry platforms.

An elastomer which exhibits the attractive properties of PDMS along with resistance to swelling in common organic solvents and chemical reagents would greatly extend the use of microfluidic devices to a wide variety of new chemical applications and other domains yet to be explored. One such application is in the synthesis of Radiopharmaceuticals for positron emission tomography (PET) imaging. Quake et al. have recently reported on the synthesis of 2-deoxy-2-[^{18}F]-fluoro-D-glucose (FDG) using a PDMS microfluidic platform.[5] While this study provides an elegant proof of concept demonstration, it is evident that improved materials are needed for this and other microfluidic platforms to reach their full technological and commercial potential.

We have previously reported on the use of PFPE – based materials in microfluidic device fabrication.[6] Herein, we describe the use of Fluorocur as chemically robust materials for microfluidic chemistry platforms including the synthesis of radiolabelled biomarkers for PET.

2 RESULTS AND DISCUSSION

2.1 Swelling Studies

To measure solvent resistance of these novel Fluorocur elastomers, tests using classical swelling measurements were performed on 5 different versions of crosslinked Fluorocur elastomers and PDMS. Sample weight was compared before and after immersion in a variety of solvents for 15 hours. The data clearly show the superiority of Fluorocur based materials in resistance to swelling by organic solvents (Figure 1). Even relatively polar solvent s such as acetone and isopropanol were found to swell PDMS significantly. The five Fluorocur materials vary in mechanical properties and cure chemistry but were

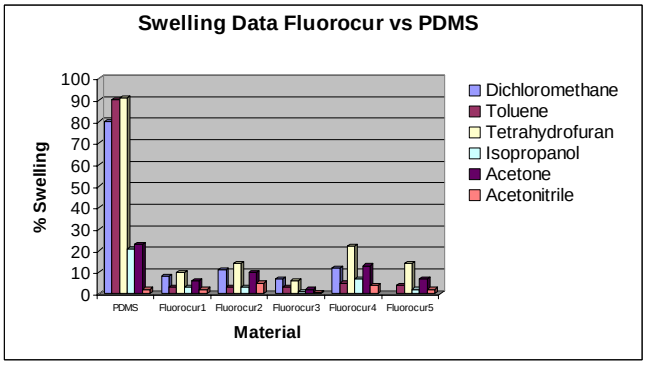


Figure 1. Swelling data for PDMS vs. Fluorocur elastomers

all found to have very low swelling in typical solvents.

2.2 Mechanical Properties

Mechanical properties of Fluorocur and PDMS materials were measured. Dynamic mechanical thermal analysis was also performed on the fully cured materials. Both the Fluorocur and PDMS networks exhibited low temperature transitions (-112 and -128 °C, respectively) as evidenced by maxima in the loss modulus. This transition accounts for the similar elastic behavior of the two crosslinked materials at room temperature. Stress strain analysis shows that the tensile modulus of the fully cured Fluorocur-based elastomer is 3.9 MPa, similar to that measured for fully cured PDMS (2.4 MPa).

2.3 Device Fabrication / FDG synthesis

Multilayer Fluorocur microfluidic devices were fabricated using modified procedures pioneered by Quake et al.[1] In this way, pneumatic diaphragm valves which controlled fluid flow were incorporated into the device (Figure 2).

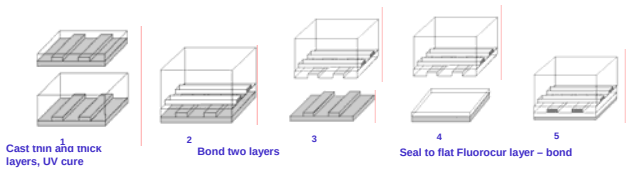


Figure 2. Schematic of device fabrication

Fluorocur layers were bonded together using proprietary methods developed by Liquidia Technologies. The adhesion was shown to be very strong, capable of holding 60 psi of pressure between layers. An example of a pneumatic valve in a Fluorocur device is shown in Figure 3.

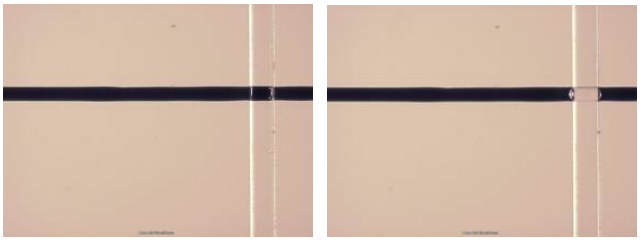


Figure 3. Actuation of pneumatic valves in a Fluorocur device

The device for FDG synthesis consisted of a reaction chamber 5mm in diameter with 8 valves controlling fluid inlet/outlet (Figure 4). A microfabricated vent was incorporated underneath the chamber which was used for solvent evaporation during the reaction.

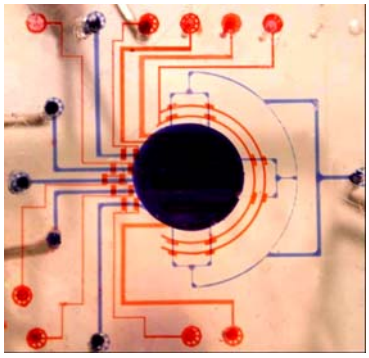
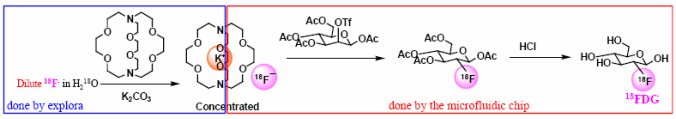


Figure 4. A Fluorocur microfluidic device used for FDG synthesis

Radiolabelled FDG was prepared in a Fluorocur device using known synthesis procedures[5] as illustrated in Scheme 1. The reaction consists of a nucleophilic attack on mannose triflate by an ^{18}F anion complexed to a potassium cryptand. The resulting protected intermediate is deprotected through an acid hydrolysis step to yield the resulting radiolabelled FDG.



Scheme 1. Synthesis of radiolabelled FDG

Reactions performed on a Fluorocur device were shown to produce radiolabelled FDG in high purity and good yield. This was in stark contrast to previous reactions performed in PDMS chips which generate fluorinated silanes through the reaction of F- with the walls of the PDMS chip.

In summary, Fluorocur microfluidic devices were shown to be chemically stable and resistant to swelling by organic solvents. Furthermore, the mechanical properties of the materials were similar to PDMS, allowing for the incorporation of pneumatic valves into the chips to control fluid flow and perform multiple functions. Fluorocur is an enabling materials breakthrough in microchemistry platforms and open the doors to many new applications which have been hindered by materials limitations.

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