ISSN: 2574-1241
DOI: 10.26717/BJSTR.2018.11.002093
Joyline Dsa. Biomed J Sci & Tech Res

BIOMEDICAL Journal of Scientific & Technical Research

Mini Review Open Access

In Vitro Characterization of Mems Based Piezoelctrically Actuated Drug Delivery Device for Biomedical Applications

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Received: November 16, 2018; **Published:** November 26, 2018

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Abstract

Implantable devices that detect and treat diseases without any intervention required from the patient are expected to be the trend of the future. This paper presents a peizo electrically controlled MEMS drug delivery device for on-demand release of defined quantities of drug in a sustained and controlled manner. A drug-loaded polymer based micro reservoir (600µm ×550µm) is sealed by a Polydimethylsiloxane (PDMS) membrane placed over the drug reservoir on which the piezoelectric material is deposited. On application of voltage across this piezoelectric material, the membrane deflects allowing the fluid to fill into the chamber that will mix with the drug and due to concentration variation; the drug would come off the reservoir or vice versa. A 0.3µm-thick PZT material is deposited on 20µm PDMS membrane. Discharge of the drug solution and the release rates were controlled by an external electric field. Characterization of the devices was implemented in-vitro using the colored water solution. The reservoir was capable of delivering 20µl drug on application of 10V.

Keywords: Polydimethylsiloxan; Drug Delivery; PZT Material

Introduction

In recent years, one of the most exciting progresses in MEMS application is the rapid evolution of Biological-Microelectromechanical systems (BIOMEMS). The BIOMEMS has gained its attention due to the microfabrication technology which has been applied to the successful development of a variety of health care related products. The research on microfabricated devices for medical application is gaining more attention. The microfabricated drug delivery system and its utility in the medical application have become a major topic of research [1-4]. In addition to basic components, such as micro channels, microvalves, micropumps, micro mixers and micro-reactors for flow management at microscopic volumes, various novel sensor and detection platforms have been reported in the micro-fluid and BIO-MEMS fields. Many of the so-called micro total analysis systems (µ-TAS) or lab-on-a-chip systems have also been reported and will offer new paradigms in biomedicine and biology, in particular, the ability to perform point-of-care measurements [5-6]. A microchip delivery system consists of a substrate which consists of fabricated reservoirs capable of holding chemicals in the solid, liquid, or gel form. The microfabrication of these devices includes numerous techniques such as lithography, thin film deposition, etching, and so on [7]. The Microfabrication technology for drug delivery system has many advantages over the traditional drug delivery approach which uses spherical drug delivery principle [8]. The use of micro technology offers a number of advantages which may modernize the field of controlled release. Microfabrication also offers precise control over shape, size, and geometry of delivery devices which in turn can increase the drug loading capacities and provide better control over drug release. Single microfabricated devices can integrate multiple reservoirs with different drug or bio-molecules and can be filled in with Pico to nanoliters of the solution, this offers a significant advantage of releasing the drug in a multi-directional way which makes it unique from the unidirectional spherical drug delivery system [9-11].

There is extensive work being carried out to use Polydimethylsiloxane (PDMS) which is considered to be bio compatible, less expensive as the main material for different drug delivery systems for cancer treatment, HIV treatment etc. PDMS based drug delivery systems can be used to achieve prolonged release profiles [12]. The drug that will be loaded into the PDMS structures can be sustained for months. The drug delivery is controlled by different actuation techniques such as diffusion or magnetic actuation [13-15]. The developed device is capable of delivering a required quantity of drug to the targeted site using

piezoelectric actuation technique. The device was actuated using piezoelectric actuation technique. This non-invasive fabricated device provides reusability, precise control and can enable the patient or a physician to actively administrate the drug as and when required.

Device Fabrication

The molds for the micro reservoirs, were made using photolithography by SU-8 2150; (MicroChem Corp., MA, USA) negative photoresist was spin-coated on a glass substrate and patterned. Cured PDMS [Sylgard 184 Silicone Elastomer, Dow Corning Corp oration] was then molded using the SU8 pattern (Figure 1). Also a 20µm thick PDMS membrane was prepared by spin coating the PDMS on the glass substrate. These reservoirs and the membrane are then treated with argon-induced plasma for 15mins and test liquid was filled in the reservoir as a sample drug. The treated membrane was then metalized (aluminium) followed by the sputtering of 0.3µm PZT layer and later evaporated for aluminium electrode using masks. The membrane was irreversibly bonded to the reservoir layer. Next, an aperture of 100*100µm 2 was drilled with a UV laser (254 nm wavelength). The bellow diagram describes the flow of the fabrication of PZT-Electrodes.

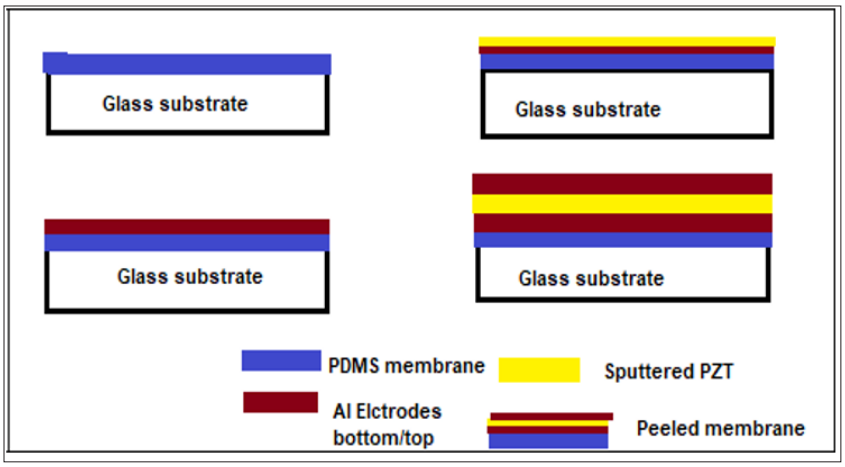

Figure 1: The membrane fabrication.

Results and Discussion

Unlike the conventional drug delivery devices, the fabricated Piezoelctrically actuated device can be used to deliver the drug to a specific target [16-18]. The PDMS membrane and the reservoir are made hydrophilic by argon plasma treatment, in order to prevent the adsorption of the drug on the PDMS surface. This surface modification is also required to have a uniform deposition of the PZT material. The fabricated device is shown in Figure 2. The device was fabricated with different membrane thickness with 5µm, 10µm and 20µm thickness. The actuation test was also carried out varying the deposition thickness of PZT for different membrane thickness. It was observed that increase in PZT thickness with constant membrane thickness results in less voltage application which is an advantage of this present device. The table shown in the below Table 1 summarizes the voltage required to actuate the device with different thickness.

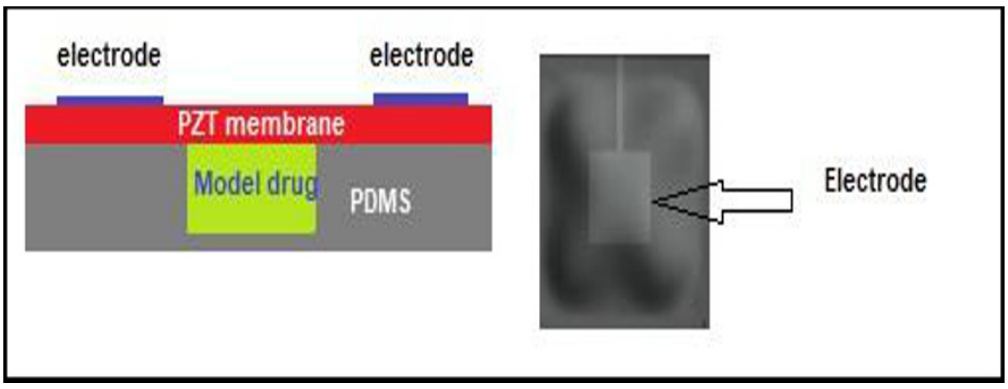

Figure 2: The cross sectional view of fabricated device and the microscopic image of electrodes.

Table 1: The voltage required to actuate the device.

PZT Thickness (um)	PDMS Membrane Thickness (µm)	Voltage (V)
0.3	5	4
	10	8
	20	30

0.5	5	2
	10	6
	20	25
0.8	5	1
	10	4
	20	16

Actuation Test

The actuation of the PZT membrane was achieved by applying variable voltages across the PZT electrodes. The device with test liquid was immersed in water. The voltage across the electrodes was slowly increased in steps. It was observed that there was permeation of the test liquid with respect to the increased voltage. it was further proven using the microscopic testing of the obtained sample with changed colour. The release of the drug is due to the deflection of the PZT membrane. The rate of drug flow was controlled by the actuation voltage. The direction of deflection of the membrane can be controlled by the direction in which electric field is applied across the electrodes. The graph in Figure 3 shows the flow of drug Vs the applied voltage. The maximum amount of the test liquid delivered was found to be 20µL. The volume of drug loaded can be varied by changing the size of the reservoirs. The purpose of this drug delivery device was to measure the drug release as a function of external actuation and not for the characterization of the drug. The percentage of cumulative drug release was calculated considering the device of PZT thickness 0.5µm and it was calculated by the below equation

$$(\%) = \times 100$$

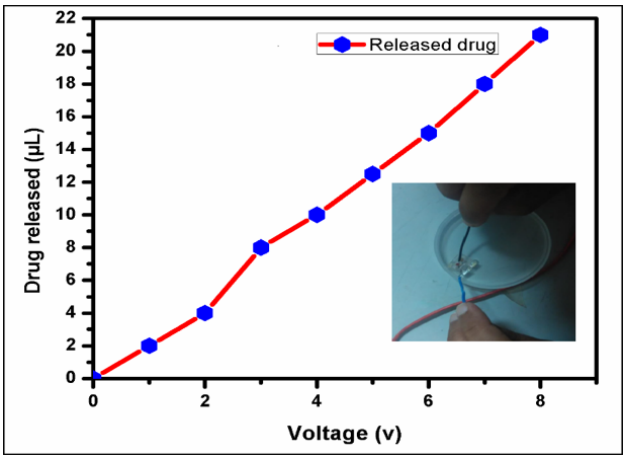

Figure 3: Graph representing the drug release with the applied field.

The graph shown in Figure 4 depicts the cumulative release of the test liquid solution with respect to the time at different voltage levels. It is observed that the time taken by the complete drug release at different voltages reduces with applied voltage. Therefore, this device finds its application at the targeted delivery of the drug where the time of release becomes an important criterion.

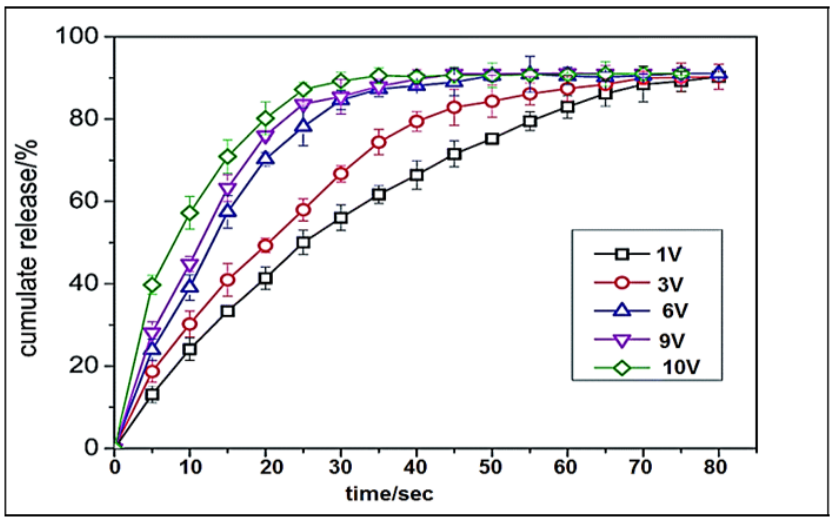

Figure 4: Graph representing the % age of the released drug with respect to time.

Conclusion

Advances in drug delivery systems have brought better control rates and increased efficacy. The developed DDS can be used for both the liquid and solid drugs. The device finds many applications where targeted and controlled delivery is required, such as protein delivery, insulin delivery, chemotherapy etc. The actuation method of the device was verified along with all the unit steps and it is concluded that increasing voltage across PZT increases the deflection of the membrane which ultimately will be used to deliver the drug into the target source. Different PZT materials with differed properties such as relative permittivity, density, can be used as electrodes for the actuation.

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ISSN: 2574-1241

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