Functional Micro-Dispensers based on Micro-Electro-Mechanical-Systems (MEMS) Integrated with Fabrics as Functional Materials to Protect Humans from Mosquitoes

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Functional Micro-Dispensers (FMDs) based on Micro-Electro-Mechanical-Systems (MEMS) were designed to deliver spatial repellents that reduce the ability of mosquitoes feeding upon humans. FMDs were integrated with fabrics as functional materials for protection against mosquito bites. The use of MEMS devices provide an unprecedented control over the release kinetics by means of integration with electronics for selective and timely activation of each device to perform controlled release of pesticides in air. Trials using transfluthrin containing FMDs improved protection against mosquito feeding in human subjects above that of permethrin-treated uniform fabric worn on the arm of the volunteer. The overall reduction in feeding was approximately 90% compared to an untreated fabric control, and about 50 % reduction compared to the permethrin-treated fabric control. The devices showed efficacy over course of 32 days weeks. FMDs could be mass produced and have the potential for a simple and cost-effective implementation for mass adoption as wearable devices integrated in fabrics as active functional materials.

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1. Introduction

This work presents the use of Functional Micro-Dispensers (FMDs) based on Micro-Electro-Mechanical-Systems (MEMS) designed to deliver spatial repellents that reduce the ability of mosquitoes feeding upon humans. FMDs were integrated with fabrics as functional materials to protect against vector bites. Recent advanced integration of drug delivery systems with MEMS and electronics have resulted in unprecedented control of release kinetic profiles for a number of unique medical applications. This new family of controlled release devices have been proposed and tested for treatment of acute conditions as well as chronic conditions. [1,2] Integration of drug delivery systems with electronics has been key for pre-programmed customization of release devices, as well as for on-demand delivery and telemetric activation via transceivers.

Vector-borne disease pose a significant challenge in human health as globally there are millions of people affected by deadly pathogens, such as Malaria and Dengue. [3,4] Current techniques to protect against medically important mosquitoes and other vectors in affected areas rely on spraying of insecticides over large areas, deployment of nets, as well as topical use of repellents [5-8]. Typically all these techniques are applied within an integrated pest management strategy to optimize protection. Current techniques for personal protection rely mainly on multiple daily topical applications of skin repellents, such as N, N-diethyl-3-methylbenzamide (DEET), or the use of permethrin-impregnated fabrics, as the last preventive step of defense [9]. Although topically applied repellents have proven to be an effective means of reducing biting from mosquitoes, its toxicity due to transdermal absorption has been previously reported as a potential risk to humans [10-12]. Recently, a number of spatial repellents have been suggested for personal use, such as transfluthrin and metofluthrin, as a means to affect airborne vectors away from the host.[13]. One of the key challenges, however, is the implementation of repellents

without the need of periodic applications, which are rendered impractical for use in large populations and in some situations. The need for compliance on the periodic application by users combined with the need to avoid transdermal absorption of toxic chemicals represent the foundations of this work. Herein, we present FMDs designed to perform controlled release from an array of reservoirs that were electronically activated. Transfluthrin was the active ingredient used to affect the mosquitoes in this study. A human trial was performed showing very promising results, as FMDs showed protection over several days.

2. Materials and methods

FMDs based on MEMS were fabricated using techniques previously presented for controlled drug delivery systems [14,15]. Each device consisted of a small cubic plastic reservoir with a 125 μ L volume. Each reservoir was loaded with transfluthrin, 100 percent concentration (Sigma Aldrich, Inc.) The reservoirs were covered by an actuator layer fabricated using microfabrication techniques, previously introduced[15]. Electro-Thermal Fuse Actuators (ETISFAs) were implemented as a silicon layer with three evenly spaced square silicon nitride membranes ($L = 70 \mu\text{m}$), covered with a narrow electric fuses accessible via flexible electrodes, as shown in **Figure 1**. The active silicon layer hermetically covered each reservoir. As a short electric pulse ($\sim 1 \text{ sec}$) was applied from a 9 V battery, the silicon nitride membranes were burst, allowing evaporation of the active ingredient. The main mass transport mechanism to release the active ingredient relied on evaporation and diffusion of the active ingredient in air.

Figure. 1

Immediately after activation, the devices were used for human trials at the Mosquito Fly Research Unit at the USDA-ARS (Gainesville, FL). Human trials consisted of testing the efficacy of five devices worn by a human subject and tested on a number of days over a period of 32 days. Laboratory tests were conducted in a small cage (approximate dimensions were: Length = 60 cm, Width = 35 cm, Height = 45 cm). The experimental design consisted of testing devices on a human arm covered with Flame Resistant Army Combat Uniform (FRACU) fabric completely sewn into a sleeve which was fitted tightly to the forearm. The hands were gloved and the worn sleeve and hand were inserted inside of a cage containing approximately 200 ± 25 female *Ae. aegypti* mosquitoes (**Figure 2B**). All mosquitoes were sacrificed and counted for blood feeding status at the end of each test. Each test was complemented by the volunteer also testing control sleeves without device. Once sleeve was not treated with permethrin (Control 1), the other sleeve was treated with a permethrin solution such that the resultant surface concentration was 0.033 mg/cm² (Control 2). This concentration was selected based on the

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amount being the typical residual permethrin concentration found on these uniforms after 50 standardized wash cycles. For the trials, FMDs were integrated into a FRACU fabric sleeve that the human subject wore, as shown in **Figure 2A**, resulting in active functional materials for preventing mosquito bites. Two FMDs were integrated in the fabric around the wrist, two FMDs were integrated at about half the length of the arm, and one FMD close to the arm end. The human purpose of the glove was to prevent bites to the hand since no additional repellent product was used to protect this part of the body (**Figure 2B**). The testing of the FMDs *vs.* controls consisted of counting number of mosquitoes that bit a human subject in a 15 minute test interval per 3 conditions: untreated control FRACU sleeve, treated FRACU sleeve, and treated FRACU sleeve with 5 devices. Tests were conducted on various days over a period of 32 days. At the end of each experiment, mosquitoes were aspirated and knocked down using CO₂ and thereafter examined on a cold table to determine whether human blood was present. This procedure allows the quantification of the number of bites that had occurred during each 15 minute trial. If a mosquito contained human blood, then it is equated with having bitten.

Figure 2.A

Figure 2. B

3. Results and discussion

In vivo results showed that the FMDs provided additional protection as evidenced by the 90 – 98 percent reduction in bites as compared to Control 1 and about 50 percent reduction compared to Control 2 (**Figure 3**). The results were normalized as a percentage of the number of mosquitoes in the cage per given set of experiments evaluated on any given day.

Figure. 3

One important aspect about FMDs based on MEMS is that the same devices were used for 32 days, demonstrating that it is possible to obtain a sustained release which remains efficacious over time. Controlled release relies on evaporation of the active ingredient through the membrane pores until the overall reservoirs are depleted. The exposed area (pore size) is proportional to the amount of active ingredient being release.

In vivo results showed the great potential of using FMDs as wearable devices against mosquitoes, which could still be used in complementarity to standard topical applications to further reduce exposure risk. Further designs will rely on simulations performed to optimize device design as a function of volatility of active ingredient, membrane permeability and environmental conditions (e.g. temperature and humidity). For future FMD generations, it will possible to include not only more devices but also large reservoirs to increase payload and overall obtain a longer time protection.

Conclusion: FMDs could be mass produced and have the potential for a simple and cost-effective implementation for mass adoption as wearable devices embedded in fabrics as the next generation of controlled release microdevices for vector protection.

The authors declare no competing financial interest

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This study was conducted with human volunteers and the procedures followed those approved by the University of Florida Institutional Review Board (IRB-01, study protocol number 69-2006).

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This study is reviewed annually. All participants provided written informed consent for their participation.

Figure captions

Figure 1. FMDs based on MEMS showing multiple components.

Figure 2. FMD integrated in fabrics resulting in active functional materials for vector control. A. Photograph of FMD integrated in fabric. B. Photograph of cage containing mosquitoes showing experimental setup. Arm is covered with FRACU fabric.

Figure 3. Percentage of mosquitoes that bit (vertical axis) in human trials conducted over a 32 day test period. These *in vivo* results compare the performance of FMDs based on MEMS (red) which reduce biting through FRACU fabric (treated at 0.033 mg/cm² permethrin) vs. the FRACU fabric (violet) without and devices. The blue line represents the high level of feeding for untreated FRACU fabric. The experiment was performed over a 32 day period. Absence of a bar for 5 devices (no red line) indicates that the human received no bites (100% protection) for that test.

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