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Towards the Development of Personalized Drug Delivery Systems Using 3D Printed Magnetically Triggerable Elastomers †

Chaolu Yan, Rodrigo Aviles-Espinosa and Elizabeth Rendon-Morales *

School of Engineering and Informatics, University of Sussex, Brighton BN1 9RH, UK; c.yan@sussex.ac.uk (C.Y.); ra408@sussex.ac.uk (R.A.-E.)

* Correspondence: e.rendon-morales@sussex.ac.uk

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Abstract: Personalized medicine is an emerging field in healthcare which aims to tailor the drug and its delivery in an individualized approach to optimize its therapeutic outcomes while minimizing its side effects. Several techniques have been developed to achieve controlled drug release. The two main technologies include active and passive devices. While passive devices can deliver the drug within a given time frame, these lack of controllability. Active delivery devices on the other hand, can be externally controlled in both time and drug volume. Besides this, they can be used as wearables representing a step forward in the quest for the development of advanced drug delivery systems. In this paper, we present the development of an externally triggered active drug delivery system showing the potential to be used in wearable devices. Our design is based on the development of a flexible magnetically triggerable resin and the use of cost-effective 3D printing technology to develop porous scaffolds containing the patient's medication. Magnetic fields in the range from 56.3 ± 1.25 mT to 167.9 ± 2.62 mT are used to control the compression of the developed triggerable elastomers to dynamically adjust the drug release patterns. The obtained results demonstrate the precise and repeatable drug delivery dosage in the range of 20.7 ± 3.5 to 102.8 ± 21.7 µL/mm demonstrating that our approach can potentially be used to develop wearable drug delivery technologies, paving the way for personalized treatments for achieving improved patient treatment outcomes.

Keywords: on-demand drug delivery; magnetic trigger; NdFeB; porous-soft materials

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1. Introduction

Personalized medicine is revolutionizing healthcare by enabling treatments tailored to individual patient needs, improving the precision and effectiveness of medical treatments. A key component of this approach is the development of drug delivery systems (DDS) that regulate medication release, optimizing therapeutic outcomes while minimizing side effects [1,2]. Traditional passive DDS, such as hydrogels and liposomes, rely on environmental triggers like temperature or pH. However, they lack from real-time control and precise adaptability, which limits their effectiveness [3].

To overcome these limitations, active drug delivery systems have emerged, providing greater control through external stimuli such as electric, magnetic fields, or light. Such systems enable real-time adjustments in drug release patterns and dosage, ensuring a personalized and precise treatment based on the patient-specific needs, ultimately improving therapeutic outcomes [4]. Wearable drug delivery systems show great promise by enabling on-demand medication release that responds to real-time physiological cues representing. This represents a significant advancement in personalized medicine aiding on its development and integration within the patients' daily lives, offering flexible and continuous medication management without the frequent involvement of the doctors once the treatment has been defined [5].

In this paper, we present the design of an externally triggered, active wearable drug delivery system. We have carried out this though the development a magnetic flexible composite resin and a cost-effective stereo lithography 3D printer to engineer magnetically porous elastomers capable of delivering precise and controlled drug release dosages in response to magnetic fields ranging from 56.3 ± 1.25 mT to 167.9 ± 2.62 mT. A proof-of-concept evaluation was performed experimentally to assess the compression ratio and the repeatability capabilities of the developed magnetically triggered drug delivery system.

This paper is organized as follows: in Section 2 the materials and methods are presented, including a description of the experimental set up. Section 3 outlines the results and discussion of the proof-of-concept experiments conducted and finally conclusions are outlined in Section 4.

2. Materials and Methods

2.1. Materials and Equipment

In this study, we used Neodymium Iron Boron (NdFeB) micro-particles having an average size of 5 μm (MQFP-B, Magnequench, Tianjin, China) to develop the magnetically loaded composite. Ferromagnetic polymers were formulated by dispersing the magnetic powders into the UV photocurable elastic resin (50–60A Shore hardness, Resione, F80, Dongguan Godsaid Technology, Shenzhen, China). The composite was loaded into a 3D printer (ELEGOO Mars Pro printer, Shenzhen, China) with a printing resolution of 47 μm on the X and Y axes, 1.25 μm on the Z axis, and a total build volume of 115 mm × 65 mm × 150 mm in the X, Y, and Z axes, respectively. A 405 nm back illuminated Liquid Crystal Display (LCD) screen with a resolution of 2560 by 1440 pixels was used for curing the composite. The scaffold was designed using Solid-Works software. As a starting point, the polymeric lattice topology was utilized and particularly the Uniform Body-Centered Cubic (UBCC) lattice geometry was selected due to its flexibility at achieving the maximum compression rate with low tensile forces comparable to those generated by permanent magnets [6].

Each scaffold block was printed with pure F80 UV resin, all having dimensions of 20 mm × 20 mm × 10 mm and 256-unit cells. The wall thickness was 2.5 mm, and the pore diameter was 0.45 mm. A cubic structure with dimensions of 20 mm × 20 mm × 5 mm was bonded into the top portion of the scaffold. This was fabricated using the developed resin composite containing 40 *w*/*w*% NdFeB magnetic particles. This preparation involved mixing the F80 resin for 2 min at 2500 rpm, heating to 45 °C to reduce viscosity, and gradually incorporating the magnetic powders into the resin. The mixture was mechanically stirred (ISTOYO, LevalIois-Perret, France) for 5 min, followed by vortex mixing (STUART SA8, IL, USA) for 3 min, and then placed in an ultrasonic bath (DK sonic, Yorkshire, UK) at 45 °C for 15 min with the aim to ensure uniform dispersion. The mixed magnetic resin was poured into a vat for 3D printing. After the printing process was completed, the scaffold was removed from the platform and cleaned with ethanol using the ultrasonic bath. The elastomers were further cured with UV light (Elegoo Mercury plus 2, Shenzhen, China) at 405 nanometers and finally dried to obtain the final samples. The printed structures were then subjected to directional magnetization using an MA-3050 system (Jiujuok, Shenzhen, China) to produce a uniform magnetization [7].

2.2. Experimental Setup

An experimental setup was designed to assess the compression ratio and the repeatability capabilities of the developed 3D printed magnetically porous triggerable elastomers. Figure 1 shows the schematic of the drug delivery systems designed to conduct the experimental evaluation consisting on:

a. A scaffold placed inside a 3D printed capsule compartment with a drug delivery aperture positioned at the proximal side of the enclosure. Figure 1(a—top) shows the

schematic representation of the uncompressed scaffold loaded with NdFeB magnetic microparticles.

b. A high precision linear stage holding the N-52 type neodymium permanent magnet (First4magnets, Nottinghamshire UK) producing a maximum magnetic field of 350 mT was manually controlled and adjusted using a micrometer stage (PT1/M, Thorlabs, NJ, USA).

c. A magnetic field meter (TD8620, HFBTE, Shenzhen, China) was used to measure the magnetic field at the surface of the scaffold. The distance between the magnet and the scaffold was defined according to the measured magnetic flux to a distance range of 0 mm to 10 mm.

d. Two CMOS cameras (FL3-U3-32S2C-CS, Teledyne FLIR, VA, USA) were positioned above the setup to capture the scaffold's deformation and record the changes produced in its width to calculate the scaffold's compression ratio under different magnetic field conditions as shown in Figure 1(a–c top).

e. A high precision digital scale with a resolution of 10 mg (PM6VSV Ascher, Shenzhen, China) was located below the aperture of the capsule compartment with the aim to weight the droplets released under the influence of different magnetic field strengths.

To conduct the experimental evaluation, the magnetic scaffolds were first hydrated by capillary action immersing these into the solution. The scaffold was then placed inside the 3D-printed capsule having a 3 mm diameter aperture to enable the drug release. The developed 3D printed magnetic scaffold sat inside the capsule filled with the drug solution which was held by the superficial tension created in each of the 3D printed scaffold pores.

The density of the liquid was estimated to be 1 g/mL which was then used to estimate the released volumes. Figure 1(a–c—bottom) shows the experimental diagram of the magnetic based drug release system showing the tree main stages of the experimental setup. Figure 1a—bottom shows the uncompressed scaffold having the magnet located within a distance of 10 mm. As the magnetic field increases due to the reduction of distance using the high precision linear micrometer stage, the magnetic scaffold is compressed as shown in Fig. 1b -bottom.

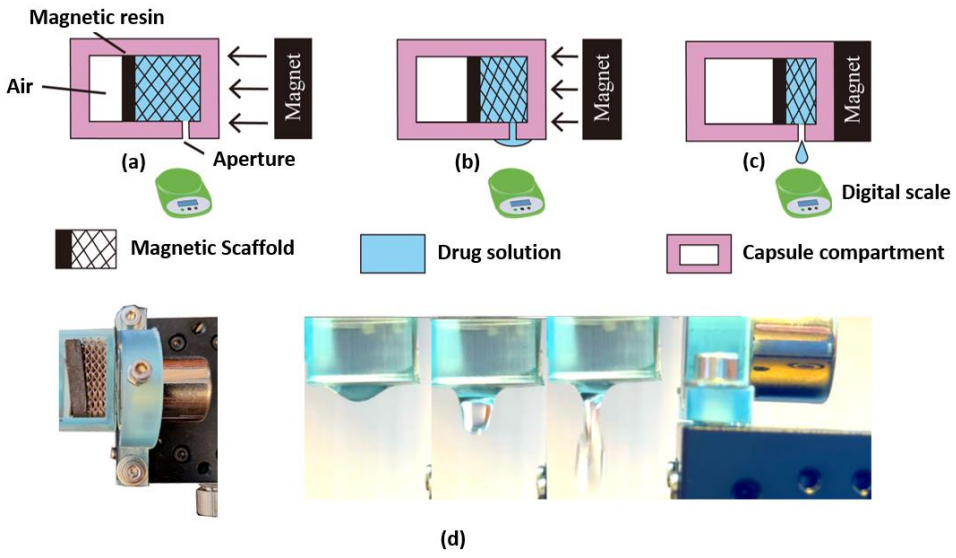

Figure 1. Schematic diagram of the magnetically controlled drug release experimental setup. (**a**) Schematic representation of the uncompressed scaffold having the magnet at a distance of 10 mm. In this setting there is no release of droplets. (**b**) Schematic representation of the compressed scaffold having the magnet positioned at a distance of 5 mm, presenting partial compression where the droplet release is dominated by the superficial tension of the liquid. (**c**) Is the schematic representation of the scaffold compression having the magnet at a distance of ~0.2 mm of the scaffold, presenting

an increased degree of compression and droplets release. The droplets were measured using the scale. (**d**) Shows the experimental setup imaged using two CMOS cameras to measure both the scaffold compression and to monitor the droplet release dynamics.

The experiments revealed that the maximum compression was achieved when the magnetic field strength reaches 167.9 ± 2.62 mT as shown in Figure 1c—bottom at a distance of ~0.2 mm. It is important to mention that there is ~ 48% reduction of the permanent magnet's magnetic field (350 mT) given that the capsule walls have a thickness of 2 mm.

The droplet release dynamics are also shown in Figure 1d—bottom. As it can be observed, as the magnetic field increases the scaffold deforms proportionally allowing the drug to be released through the pores and capsule aperture, thus regulating its dose based on the magnetic field strength.

3. Results and Discussion

To evaluate the precision and the repeatability capabilities of the developed 3D printed magnetically porous triggerable elastomers using the experimental setup described in the previous section, two experimental tests were carried out:

I. Assessing the compression ratio of the scaffold located inside the drug delivery capsule affected by different magnetic field strengths.

II. Quantification of the mass and associated volume of the droplet released considering the density of the employed liquid.

Figure 2a illustrates the relationship between magnetic field strength and the scaffold compression ratio obtained from experiment I.

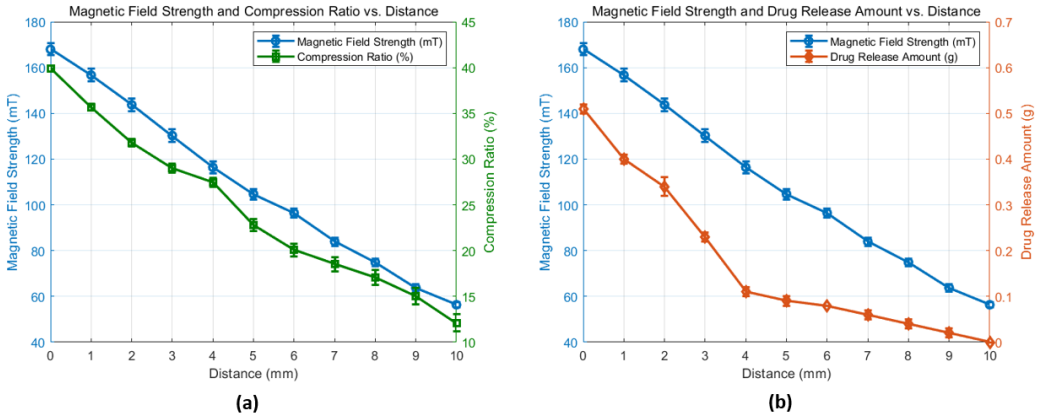

Figure 2. (**a**) Experimental results of magnetic field strength versus the distance variation of the neodymium permanent magnet and 3D printed scaffold compression ratio. (**b**) Experimental results of magnetic strength vs. drug release mass resulting from the distances variation between the permanent magnet and the scaffold.

During the experimental tests to assess the compression ratio of the scaffold, the results showed that the magnetic field strength is directly proportional to the scaffold compression obtained. As the distance between the permanent magnet and the scaffold is decreased from 10 mm to 0 mm, the magnetic field strength acting on the scaffold increases from 56.3 ± 1.25 mT to 167.9 ± 2.62 mT, resulting in a compression ratio increase from 12.12 ± 0.93% to 39.90 ± 0.3%. This key finding is required for obtaining information about the compression dynamics of the scaffold to develop a predictable compression model (i.e., a linear expression) which can then be associated to the release of the liquid and therefore determine the amount of drug released as a function of the applied magnetic field with de goal of accurately delivering a specific amount of medication to the patient.

On the second experiment the drug release amount increased in a quasi-linear proportion as the magnetic field strength was increased from 56.3 ± 1.25 mT to 167.9 ± 2.62 mT. Figure 2b shows this relationship. To illustrate the drug release patterns, when the

magnet is positioned within the middle of the total travel range (i.e., 5 mm) the droplets released weighted in total 0.09 g, however when the magnet was positioned at 0.2 mm from the capsule and the scaffold experienced maximum compression the released droplets weighting 0.51 g in total.

Moreover, the obtained experimental data enables observing that within the initial increase of the magnetic field strength i.e., considering the distance from 10 to 5 mm the release volumes are 20.7 ± 3.5 μL/mm. However following such initial scaffold compression, the remaining liquid distribution may be held within the middle to top pores therefore requiring higher compression and thus higher magnetic field strengths. This resulted in the release of higher drug volumes in the range of ~ to 102.8 ± 21.7 μL/mm as shown in Figure 2. These experiments suggest that through the adjustment of the magnetic field strength, the amount of drug released can be controlled, facilitating a personalized drug delivery having the potential to be embedded on a wearable device.

4. Conclusions

In this paper, we have presented the development of an externally and magnetically triggered 3D printed scaffold embedded in a 3D printed capsule for drug delivery applications.

This was carried out by formulating a novel magnetic flexible resin based on NdFeB magnetic particles that were used to develop 3D printed porous scaffolds using a conventional 405 nm photolithographic 3D printer. A remote triggering system was developed based on a Neodymium permanent magnet considering the decay of the magnetic field as a function of distance producing magnetic fields in the range of 56.3 ± 1.25 mT to 167.9 ± 2.62 mT at the surface of the scaffold. A high precision liner stage was used to control the distance and thus the variation of the magnetic field strength applied to the scaffold. This was used to compress the developed magnetic drug delivery device having a linear and repeatable compression.

This resulted in a precise drug delivery where the developed device was able to deliver precise drug quantities in the range of 20.7 ± 3.5 to 102.8 ± 21.7 μL/mm. Thus, the system demonstrated precise dosage control, paving the way for more effective patient-specific drug delivery solutions. This research contributes to the advancement of personalized medicine by enhancing the precision and adaptability of wearable drug delivery technologies.

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