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A Strain-Regulated, Refillable Elastic Patch for Controlled Release

Bongsoo Kim, SangHyuk Yoo, Yong-Jin Kim, Jaeyoon Park, Byunghoon Kang, Seungjoo Haam, Sun-Woong Kang, Keonwook Kang, and Unyong Jeong**

Many stimulus-induced release systems have been studied for the smart control of drug delivery. Mechanical strain is rarely investigated as means of stimulation for these systems, despite the fact that there are many biological processes and human body motions that involve strain changes. In this study, a design for a stretchable reservoir-based patch-type release system is suggested. The reservoir made of an elastomer undergoes a decrease in volume when the system is deformed by bending and stretching. The response is predicted by finite element method modeling studies. The release rate of the reservoir is finely controlled by attaching elastic microchannels with different channel lengths. Because the whole system is made of rubber, the patch is deformable and the solution can be refilled with a microsyringe. Systematic designs for on/off release, long-term release, and short-term release are suggested.

1. Introduction

Many clinical situations that involve drug delivery require smart control of the drug release pattern. Sensitive responses to physiological changes or external stimuli can enable real-time control over the dosage,[1,2] which is most desirable when it occurs as a simple prolonged, continuous release.[3,4] A variety of stimuli have been studied for smart release control, including pH,[5,6] temperature,[7,8] ultrasound,[9,10] and electric[11,12] or magnetic fields.[13,14] However, studies on release control regulated by mechanical strain are less common.[15–19] This is despite the fact that there are many processes involving strain changes in the human body and other biological systems, such as compression in cartilage and bone, tendon and muscle tension, internal shear force in blood vessels, and external force applied to skin.[20]

Patch-type release is a promising system that can respond to mechanical stimuli and be implanted in the body or mounted on human skin.[21–24] There have been several patch-type approaches to strain-regulated delivery in the past, many of which were based on mechanochemical changes[16,25,26] or on strain-responsive leakage from microcapsules,[18] hydrogels,[19,27] or reservoirs containing microchannels.[17] For precise release control over a long period of time, a reservoir-based release system with a microchannel is advantageous because the release rate is dependent on the dimensions of the outlet channel, which can be readily adjusted by simple lithographic techniques. Advanced patch-type release systems are expected to possess the on/off regulation for fine release control and the stretchability to incorporate body motions. Refilling of the drug solution may help long-term use of the patch system. Currently, most systems in this category rely on pressure[15–17,19] as a release stimulus; however, strain is a more logical choice of stimulus than pressure for human body applications because many body motions (such bending, twisting, and stretching) involve large amounts of strain.

This study suggests designs of stretchable refillable patch-type systems in which the release is regulated by external strains. As a proof-of-concept, the system was made of an elastomer, poly(dimethylsiloxane) (PDMS). The reservoirs were connected through microchannels for fine control of the release rate. The decrease of the reservoir volume caused by external strain was predicted by nonlinear finite element method (FEM) calculations.

2. Result and Discussion

The strain-regulated patch in this study contains an array of uniformly sized spherical reservoirs located just below the top surface of a rubber substrate. PDMS was chosen as the

Dr. B. Kim, Dr. Y.-J. Kim, Dr. J. Park
Department of Materials Science and Engineering
Yonsei University
134 Shinchon-dong, Seoul 120-749, Korea
S. H. Yoo, Prof. K. Kang
Department of Mechanical Engineering
Yonsei University
134 Shinchon-dong, Seoul 120-749, Korea
E-mail: kwkang75@yonsei.ac.kr
B. Kang, Prof. S. Haam
Department of Chemical Engineering
Yonsei University
134 Shinchon-dong, Seoul 120-749, Korea
Dr. S.-W. Kang
Korea Institute of Toxicology
141 Gajeong-ro, Yuseong-gu, Daejeon 305-343, Korea
Prof. U. Jeong
Department of Materials Science and Engineering
Pohang University of Science and Technology
77 Cheongam-Ro, Nam-gu, Pohang 120-784, Korea
E-mail: ujeong@postech.ac.kr

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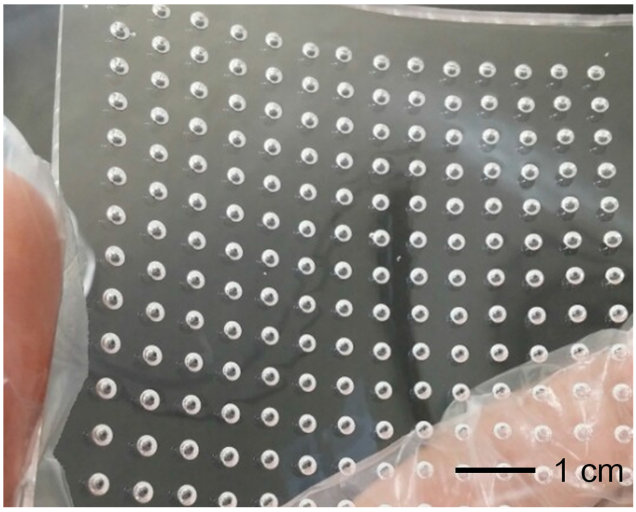

Figure 1. An array of the deformable spherical reservoirs prepared with an automated dispenser. Water droplets were dropped on the PDMS prepolymer solution and the PDMS was thermally cured.

substrate rubber because it is biocompatible and does not cause skin irritation.[28,29] An array of spherical reservoirs was formed by dropping water (4.2 µL per drop) through an automated dispenser on a PDMS mixture liquid (19 mL, Sylgard 184, Dow Corning) in a petri dish (10 cm in diameter). An array of spherical reservoirs (8×8 cm^2) could be readily fabricated (**Figure 1**). The mixing ratio of the PDMS monomer and the curing agent was 10:1 (w/w). The density of the PDMS liquid (1.03 g mL^{-1}) at room temperature is higher than the density of water (1.00 g mL^{-1}), so the water drop floated on the PDMS surface but was also partially submerged in the PDMS liquid. The water droplet formed a small opening (0.4 mm in diameter) measured from the dotted line indicated in **Figure 2**A. Based on the force balance between the gravity and the buoyancy of water, 3% of the water volume should be remained above the PDMS surface. From this calculation, the opening diameter is predicted to be 1.2 mm. This discrepancy comes from the spreading of PDMS on the water droplet. The spreading coefficient (S) of the PDMS liquid on water can be calculated using Equation (1) as follows

$$S = \gamma_{\text{water-air}} - (\gamma_{\text{water-PDMS}} + \gamma_{\text{PDMS-air}}) \quad (1)$$

where γ is the interfacial energy at each interface ($\gamma_{\text{water-air}}$ = 73 mN m^{-1}, $\gamma_{\text{water-PDMS}}$ = 42.7 mN m^{-1}, $\gamma_{\text{PDMS-air}}$ = 21.3 mN m^{-1}).[30] The value of S was 9 mN m^{-1} and hence the PDMS liquid spread on the water and decreased the opening size as illustrated in Figure 2B. The opening size (R_{open}) was dependent on the size of the water drop (R_{d}), as plotted in Figure 2C. The ratio $R_{\text{open}}/R_{\text{d}}$ increased linearly with R_{d} with a slope of 0.2, and hence $R_{\text{open}} \approx 0.2\ R_{\text{d}}^2$. With these parameters, the spread of the PDMS liquid was balanced with the gravity of the spreading liquid (see detailed mathematical derivation in the Supporting Information). In this study, R_{d} was varied in the range of 0.2–1.2 mm. It is notable that cylindrical cavities are easier to construct than the spherical cavities in this study. However, thin cylindrical reservoirs often cause

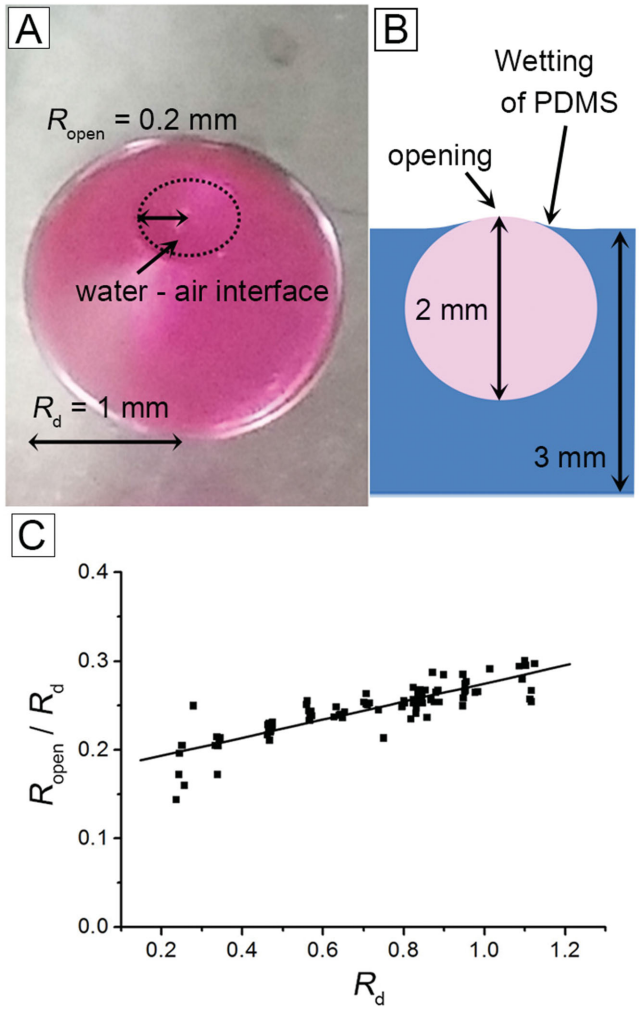

Figure 2. A) A photograph of a water droplet on the PDMS prepolymer solution. A small area of the water droplet was not covered and a small opening was created. B) A schematic illustration showing the cross-sectional view of the water droplet on the PDMS prepolymer solution. The PDMS liquid spreads on the water drop. C) The ratio of the opening radius (R_{open}) to water droplet radius (R_{d}) as a function of R_{d}. The average slope was about 0.2.

considerable amount of drug solution left in the reservoir, especially at the corner of the cylinder bottom. This loss of drug results from the uneven distribution of the strain in the cylinder by the deformation of the reservoir. The spherical reservoir creates more uniform strain distribution around the outlet of the reservoir, hence the release from the reservoir can be close to 100% as long as the outlet is at the top of the reservoir.

Figure 3A schematically describes the procedure to fabricate a strain-regulated release system. Water droplets were placed onto the PDMS mixture liquid through an automated dispenser. The PDMS was cured at 70 °C for 3 h in a dry oven, and an array of spherical reservoirs with a small opening was created by evaporation of the water droplets. It was found that the volumes of the water droplet and the reservoir were the same. In order to control the release rate, a microchannel was constructed on each spherical reservoir. A PDMS film with

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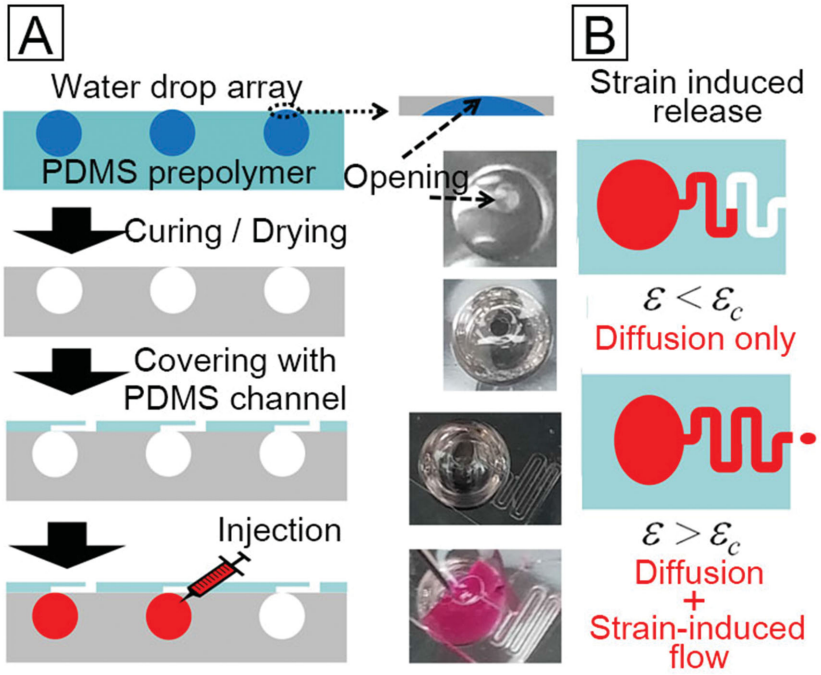

Figure 3. A) The fabrication process of an elastic patch with an array of reservoirs. Drug solutions are refillable in the elastic patch. B) The effect of the microchannel in the drug release from the elastic reservoir. Drug molecules are released by diffusion only when the deformation of the reservoir is not enough ($\varepsilon < \varepsilon_c$). If the strain is large enough, ($\varepsilon > \varepsilon_c$), the strain-induced flow governs the release rate.

an array of indented zig-zag line patterns was adhered to the PDMS substrate containing the reservoirs. The PDMS film with the indented line pattern was prepared by spin-coating the PDMS mixture liquid on a SU-8 master mold, followed by cross-linking and peeling-off of the template.[31–33] A hole was made at the end of each microchannel for use as a drug release outlet. Oxygen plasma (50 W, 30 s) was applied to both the PDMS film and the PDMS substrate with the reservoirs, which were then held together with gentle pressure. The ends of the indented lines were aligned to be positioned on the opening of the reservoirs, and then the two PDMS substrates were welded together using this plasma-assisted process.[28,34] A solution containing drug molecules was injected in the spherical reservoir using a needle.

Figure 3B illustrates the concept of strain-regulated release as examined in this study. Drug molecules continue to diffuse out through the microchannel even without any mechanical stimulation. The release rate by diffusion can be adjusted by controlling the channel cross-section (A) and length (l) of the microchannel. In this study, the length of the microchannel was varied in the range of 3–14 mm, and R_d was varied in the range of 0.2–1.2 mm (Supporting Information Figure S1). One extreme for this type of system is to have no diffusional release through a long channel with a small cross-section. For example, when $A < 100\ \mu m^2$ and $l > 10$ cm, only 10 ng of molecules can diffuse out from a 0.1 wt% drug solution in water (according to Fick's first law). The other extreme is immediate diffusion when $l = 0$. In an ideal case, the channel dimensions should be designed to meet the release rate of target drugs, whether a given drug requires a complete on/off delivery control or a continuous slow diffusion with occasional pulse releases. The microchannel acts as a buffer to the drug release; when the volume of the reservoir is reduced by external strain, the drug solution in the reservoir is pressurized to flow through the microchannel. If the volume decrease of the reservoir (ΔV_R) is smaller than the total volume of the channel (V_{ch}), the drug solution cannot leak out of the channel and it flows back to the reservoir when the pressure applied to the reservoir is removed. Therefore, a critical strain (ε_c) is necessary to generate strain-induced drug release. Once $\Delta V_R > V_{ch}$, or when $\varepsilon > \varepsilon_c$, the release is governed by mechanical stimulation.

Because the system in this study is completely composed of elastomer, it can be deformed to a high degree without suffering any permanent damage (**Figure 4**A). Conformal contact of the patch to the skin and its affine movement according to the deformation of the skin have attracted increasing interest. This deformability of a patch is considered as a basic mechanical property for use as a skin-mounted or body implanted patch because such a patch could maintain adhesion due to the affine deformation along the deformation in human body.[35,36] In addition, drug solutions may be refilled in the reservoir through the elastomer wall by using a microsyringe (Figure 4B). The dye molecules remained in the needle made a staining line of dye color in the elastomer wall while the needle was pulled out. Since the highly elastic reservoir wall filled the stained line, no leakage was observed during repeated mechanical bending tests. The possibility of refilling drugs has been studied continuously.[37,38]

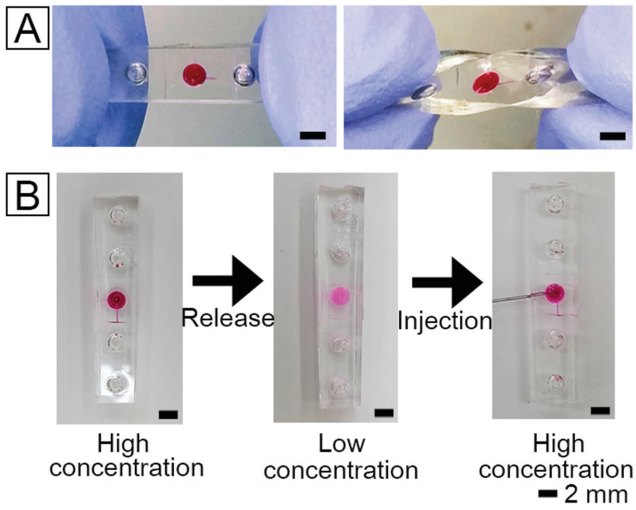

Figure 4. A) The mechanically deformable elastic patch. B) Refilling of the drug solution with a needle through the elastomer patch. All scale bars are 2 mm.

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The refillable drug reservoir enables greater utilization of drug solutions and allows various combination therapies. Frequent replacement of drug systems on the skin may cause acute bacterial infections, and implanted systems require repeated surgical interventions. If a delivery system requires only a single surgical intervention and be refillable, it can improve patient compliance and reduce associated risks.

As previously stated, the primary goal of this study is to suggest a design for a patch-type release system in which the release profile can be regulated by the strain caused by human body motions. To that end, the relationship between bending motions and the amount of release from the system was investigated. Bending of the body involves both deflection and extension, which is why the substrate should be elastic. **Figure 5** shows the volume change of the reservoir (ΔV_R) as a function of the bending radius (r). The bending radius was controlled with a plastic template (Figure 5A). The patch was placed in the inner wall of the plastic template. The bending radius was measured from the bending curvature of the plastic template. The shape of the deformed reservoir observed in the experiment was similar to the shape predicted from the second-order Ogden model (Figure 5B), where the parameters for PDMS were obtained from a previous report.[39] The spherical reservoir was deformed to be tear-shaped after bending. The relationship between reservoir volume change and the bending curvature ($1/r$) demonstrates a trend that was qualitatively similar to the released amount measured experimentally (Figure 5C). The simulation prediction for r = 19 mm in Figure 5C underestimates the measured release amount. This mismatch comes from the crumpling of the opening area by the large deformation, which occurs because the opening area is covered with only the PDMS thin film containing the microchannel.

Figure 6A–C exhibits the accumulated release profiles of the patches when bending was exerted on each specimen at different bending radii: (A) 45 mm, (B) 27 mm, and (C) 19 mm. The release tests were conducted in a phosphate-buffered saline (PBS) buffer solution (3 mL). The setup for this release test was shown in Supporting Information Figure S2. The specimens were dipped in the PBS buffer solution for 10 min, and bending was maintained for 1 min. The bending events are indicated by the arrows. An aqueous solution of rhodamine B (0.01 wt%, 4.2 µL) was injected into the reservoirs of a given patch and used as an indicator to check the amount of material released. The PBS buffer solution was taken and used to obtain intensity of fluorescent. The release profile of the rhodamine B solution depends on the relative fraction $\left(f_{ch} \equiv \frac{V_{ch}}{V_R} \times 100(\%)\right)$ of the channel volume, which in turn depends on the reservoir volume (V_R) as well as r. The microchannel volume fraction was varied at f_{ch} = 0%, 2%, 4%, and 9%. When f_{ch} = 0%, the amount of material released by bending was prominent, as was the leakage caused by diffusion. Including the bending-induced release and diffusional release, the % release after three times of bending events at R = 19 mm was 22% at f_{ch} = 0% and 3% at f_{ch} = 9%. The maximum releases from the systems were similarly about 70%. The number of bending to reach the maximum release was varied according to the f_c; for instance at R = 19 mm, 10 bending events at f_{ch} = 0% but more than 100 times bending events at f_{ch} = 9%. These results indicate that the release rate

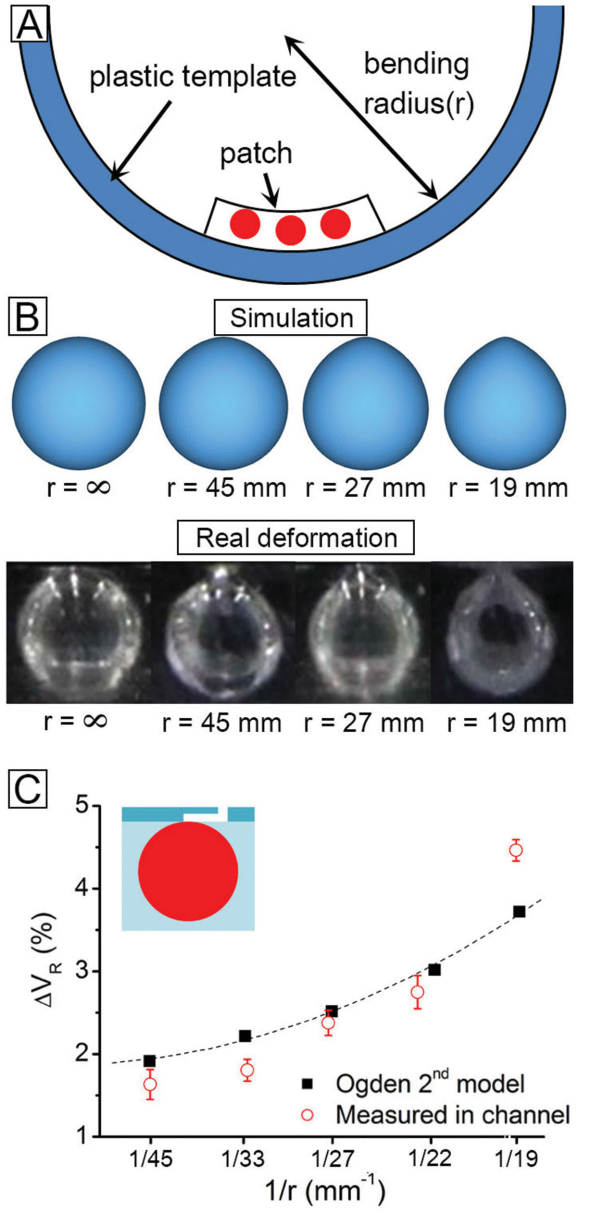

Figure 5. A) Scheme of the bending test. The patch sample is on the inner wall of a flexible plastic template. B) Simulation by the finite elemental method (FEM) using the second-order Ogden model for bending deformation of the elastic reservoir, and its corresponding experimental observation at the same bending radius. C) Volume decrease of the reservoir (ΔV_R) according to the inverse bending radius. The black dot and line indicate the FEM prediction and the red circle indicates the real measurement. The volume change was obtained by measuring the length of the liquid filled in the microchannel.

can be adjusted to meet the target applications. Fine release control over long time period is critical in implanted systems. For the patches used as a transdermal delivery, the refilling of the drug solution is a way to achieve % release close to 100%, which is important for expensive drugs. Figure 6D summarizes the released amount by one given bending event as a function of f_{ch}. As an example at R = 19 mm, the released amount per each bending varied from 4% at f_{ch} = 0% to 0.3% at f_{ch} = 9%.

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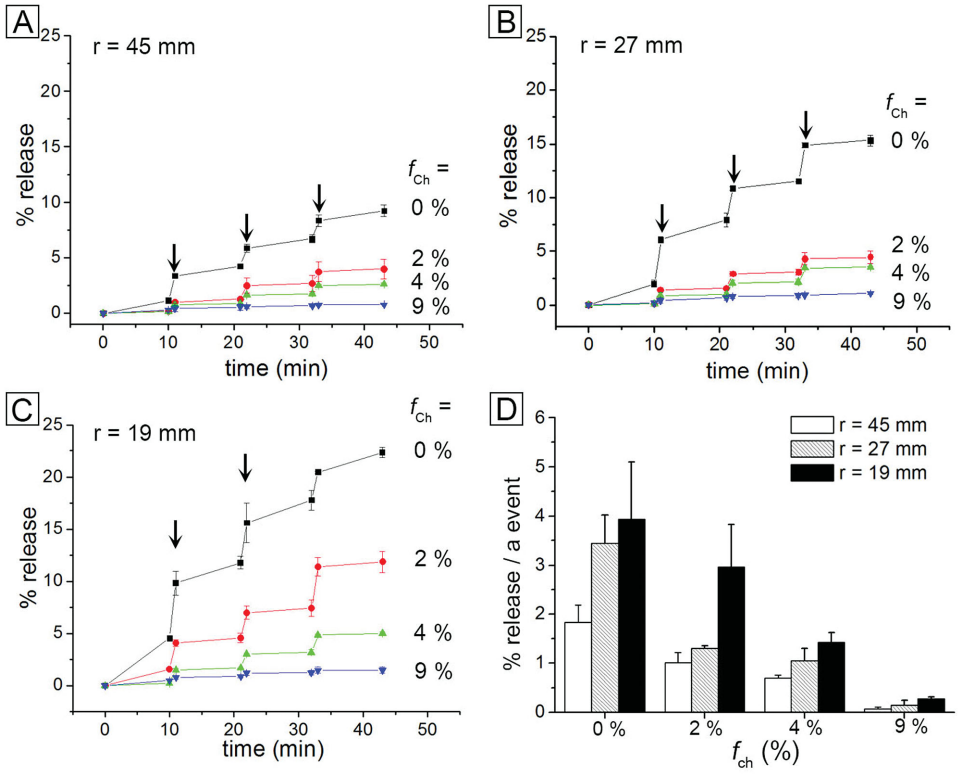

Figure 6. Release profiles according to the bending radius (r) and the volume fraction of microchannel (f_{ch}) versus the volume of the reservoir. The bending radii are A) $r = 45$ mm, B) $r = 27$ mm, and C) $r = 19$ mm. D) The average amount of released dye (rhodamine B) per bending event.

The release at bending was reduced as f_{ch} was increased, which is due to the critical ΔV_R similar to the channel volume (V_{ch}). The microchannel effectively reduced the diffusional leakage as well. The amount released by the external strain depends on V_{ch}, and the diffusional leakage was controlled mainly by the cross-sectional area of the microchannel; these are the two parameters that can be adjusted to meet the desirable release profile of a target application. The release test in this proof-of-concept study was conducted in the water medium. Water could flow in the channel when the press on the reservoir was released, so no droplet caused by the air trap was observed. When the release should be conducted on the skin without enough moisture, the reduced volume of the reservoir was filled with air and the air trap was observed in the channel. Making a small hole on the top surface of the reservoir on which pressure is applied prevented the air flow through the channel and allowed air flow through the small hole, hence no droplet of drug solution was observed in the channel.

If the release rate could be controlled independent of the total reservoir volume, such behavior would make these systems even more attractive for drug release applications over extended time periods. The reservoir volume cannot be too large because a thick patch loses its softness and becomes unable to maintain good adhesion to the skin. Therefore, a thin elastic reservoir is desirable for deformable patches, which was obtained in this case by connecting the reservoirs with a microchannel as shown in **Figure 7**A. A PDMS film containing a microchannel was attached across two neighboring reservoirs, and the microchannel was positioned to connect the openings of the reservoirs. Since the pressure difference between the two reservoirs is small in this setup, when identical strain was applied to the reservoirs, the flow of the solution from reservoir *A* to reservoir *B* was not significant compared to the volume decrease of a single reservoir. The release rate during deformation was determined from the ratio of the volume fraction (f_{ch}) of the outlet microchannel and the volume of the reservoir connected to the outlet channel. Therefore, the release rate in the connected setup is half the sum obtained from two isolated reservoirs with the same microchannels (Figure 7B). Connecting the reservoirs has a variety of additional useful benefits. Undesirable release by diffusion can be effectively reduced in this setup. In addition, because the drug molecules diffuse from reservoir *A* to reservoir *B*, any rapid concentration drop in the outlet reservoir (*B*) can be prevented. Lastly, the release of multiple drugs can be programmed by injecting different drug solutions in the reservoirs. The two drug molecules would be released in a mixed state, but the drug in reservoir *B* will be first released dominantly, and the other drug in reservoir *A* will be released dominantly after a certain time. Connection of two or three reservoirs was aimed in this study for refilling at once. Refilling the whole patch containing a large number of reservoirs needs an automated system which is not developed yet as long as our knowledge concerns.

All the above-stated release tests were conducted with inward bending. However, those systems are responsive to outward bending, too. Although we can use this response to control the drug release, it can cause an unexpected release in practical uses. With a proper design of a responsive system that

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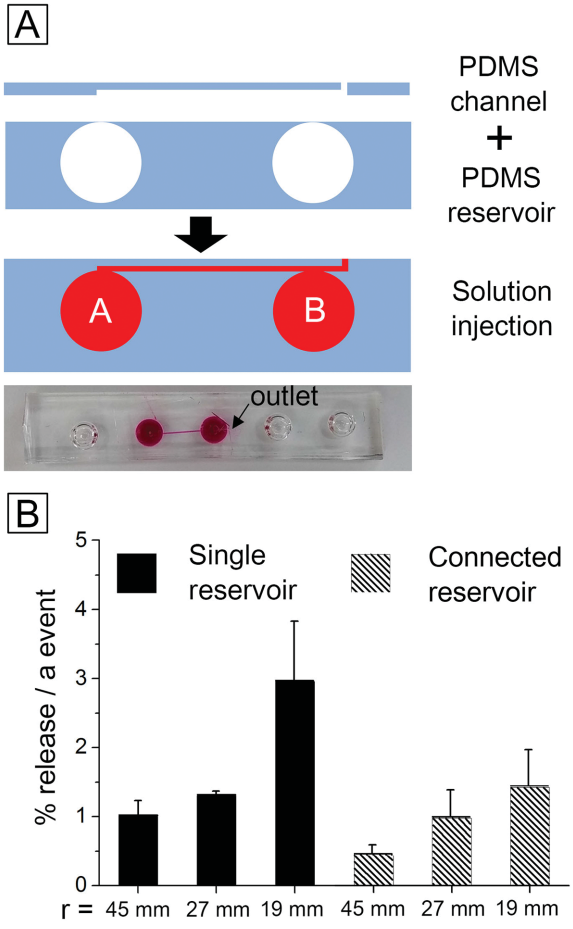

Figure 7. A) The process to fabricate connected reservoirs with a microchannel. Two connected reservoirs have one outlet microchannel on the reservoir *B*. B) Comparison of the % release per bending event from a single reservoir and from the connected reservoirs.

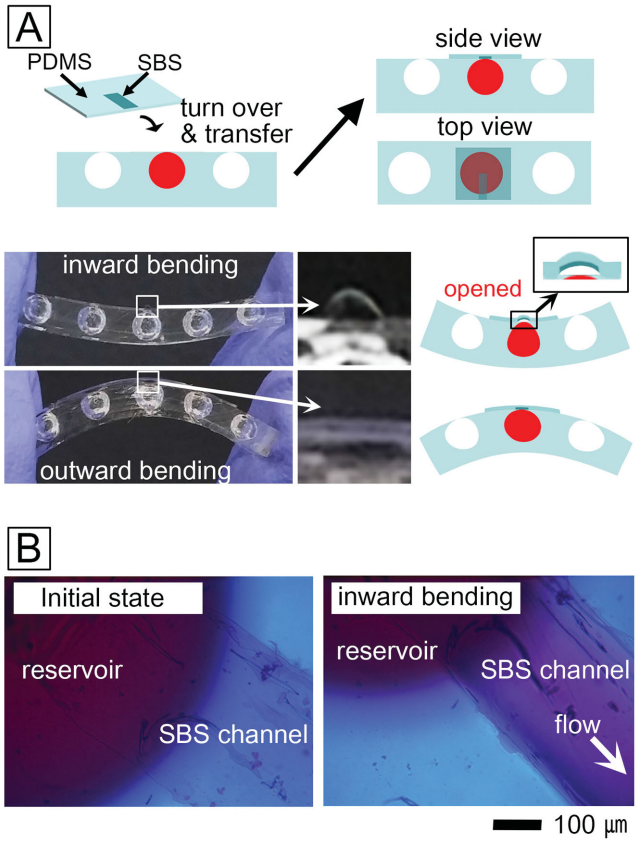

Figure 8. A) The process to fabricate the on/off system on the PDMS reservoir. A PDMS film containing a square SBS pattern on it was covered on the reservoir. With inward bending, the SBS pattern on the reservoir was dethatched. B) The rhodamine B solution flows out through the on/off system when inward bending is applied.

is responsive to inward bending only, we can fabricate a more stable patch-based drug delivery system. **Figure 8** shows an on/off system that turns off the release when the system is bent outward. A PDMS film was formed on a slide glass and treated with oxygen plasma. A poly(styrene-*b*-butadiene-*b*-styrene) (SBS) solution dissolved in chloroform (3 wt%) was spin coated on a rectangular PDMS stamp (width of 300 μm, length of 1 mm). The rectangular SBS pattern on the PDMS stamp was transferred to the PDMS film on a slide glass by annealing at 150 °C. The PDMS film with the rectangular SBS pattern was covered on an oxygen-plasma-treated PDMS reservoir. The rectangular SBS pattern was positioned on the reservoir opening. The PDMS film and the reservoir had been treated with oxygen plasma before making contacts. Contacting the plasma-treated two PDMSs led to strong welding so that they were not detached by fingers. It is notable that the SBS pattern and the reservoir have no adhesion. When the inward bending was applied, the SBS pattern could be detached from the PDMS reservoir and make connection to the microchannel; hence, the drug solution can flow out ("on" state) (Figure 8A). On the contrary, when the outward bending is applied, the SBS film is stretched and maintains tight interface with the reservoir, so the opening of the reservoir is blocked and no flow is allowed ("off" state). Figure 8B shows the "on" state of this reservoir, at which the solution flew out through the channel under inward bending.

The releasing amounts from the on/off system under inward bending and outward bending were plotted in **Figure 9**. The accumulated release profiles are given in Supporting Information Figure S3. Generally, the releasing amount was proportional to decrease of bending radius (harder deformation). The releasing amount without any motion did not change with time, which indicates that the small released amount in Figure 9 was a leakage caused when the specimen was dipped in the buffer solution. The releasing amount under inward bending from the on/off system was slightly larger than that under inward bending from the microchannel system (V_{ch} = 2%). The releasing amounts from the microchannel system were 3.0% at r = 19 mm, 1.3% at r = 27, and 1.0% at r = 45 mm, and those from the on/off system were 4.1% at r = 19 mm, 2.0% at r = 27 mm, and 1.2% at r = 19 mm. This difference is because there is no buffer space in the on/off system so that the liquid entry is easier than in the microchannel system. A big difference was observed under outward bending. The drug solution was released out (last column in Figure 9) under outward bending from the microchannel system, meanwhile no

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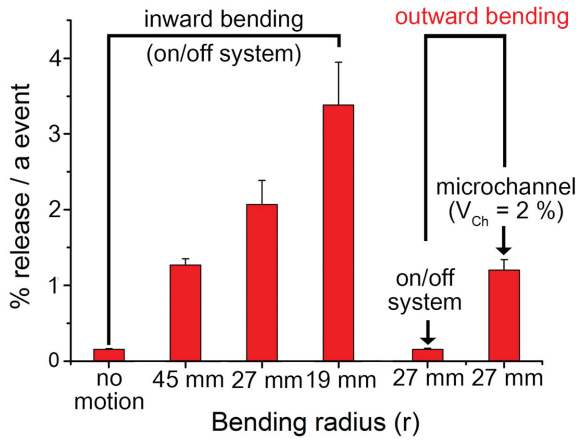

Figure 9. The % release from a bending event with inward bending and outward bending. With outward bending, the solution was released from microchannel containing reservoir (V_{ch} = 2%) but the solution was not flowed out from the on/off system. The first column (no motion) indicates release amount in 10 min without bending motion. All data are obtained from three samples in each condition.

release was detected from the on/off system except for the small leakage caused when the specimen was dipped in the buffer solution. The repeated outward bending did not activate the release from the on/off system.

This study has focused on the design of strain-regulated stretchable delivery system. Although we checked the released amount with a hydrophilic organic dye, the system is applicable to hydrophobic drug molecules because they follow the similar release profile which depends on the reservoir volume and channel volume fraction. The overall thickness of the current patch is to be reduced to less than 2 mm which is industrially fine for transdermal delivery patches. We pursue a quantitative transdermal delivery regulated by fine control of normal pressure applied on the delivery patch. The system is a combination of E-skin pressure sensor, stretchable delivery patch, and microneedle fabrication. The key to the success is to find quantitative correlations among the external force applied on the patch, deformation degree of the reservoir, released amount of drug solution, and the penetrated amount of drug through the skin. This system is considered to be beneficial to the neurological disorders such as Alzheimer's disease because the drugs for the diseases are known to be most effective by transdermal delivery.[40]

3. Conclusion

A convenient method to fabricate strain-regulated patch-type drug release systems made entirely of an elastomer, which are deformable and refillable, was proposed in this study. Water droplets coming out of an automated dispenser were placed on a PDMS prepolymer mixture solution, and spreading of the PDMS liquid made a small hole on the water droplet. Thermal curing of the PDMS mixture generated an opening on top of the reservoir with predictable sizes. The volume of the reservoir was shown to shrink as a result of external bending deformation. The FEM-based predictions of the volume decrease caused by bending deformation were in good agreement with experimental measurements. The microchannel attached to the opening of the reservoir acted as a buffer to reduce the diffusional leakage and control the release rate of a test drug solution. By adjusting microchannel volume fraction (f_{ch}), fast release could be obtained at small f_{ch} by only several bending events, whereas slow release was achieved at large f_{ch} even after a large number of bending events. In addition, a system showing complete on/off regulation under inward bending was demonstrated. The concepts suggested in this study for fabricating strain-regulated stretchable patches can be applied in production of practical drug delivery systems.

4. Experimental Section

Materials: PDMS (Sylgard 184) was purchased from Dow Corning, and SU-8 50 was purchased from MicroChem. Rhodamine B was purchased from Sigma-Aldrich.

Fabrication of Spherical Reservoirs: The PDMS prepolymer mixture was poured into a petri dish with a depth of 3 mm and a diameter of 10 cm. The PDMS prepolymer and curing agent were mixed in a 10:1 ratio (w/w). Water droplets (4.2 μL, 2 mm diameter) were dropped on the PDMS prepolymer mixture at intervals of 5 mm. An automated dispenser (300 DS-S, Musashi) was used for precise control of the volume and distance between the drops. The water droplet array in the petri dish was covered with a lid and heated at 50 °C on a hot plate for 2 h to cross-link PDMS. The dimension of hollow sphere was maintained during curing. The PDMS was annealed at 80 °C for 12 h in a heating oven for complete curing.

Fabrication of the Outlet Channel: A master mold with a zig-zag embossed line was made with SU-8 using conventional photolithography processes.[28–30] All microchannels had a height of 100 μm and a width of 250 μm. The length of the microchannel was varied in the range of 3–14 mm, and the channel volume (V_{ch}) was varied in the range of 0.09–0.37 mm^3 as a consequence (Supporting Information Figure S1). The PDMS prepolymer mixture was spin-coated on the SU-8 master mold at 500 rpm for 20 s and it was cured at 80 °C for 6 h. The cured PDMS film with the outlet channel was detached from the master mold, and oxygen plasma (Cute-B, Femto Science, Korea, 50 W for 30 s) was applied on both the PDMS film with the channel and the PDMS patch with the reservoir. The two PDMSs were attached and pressed by hand and were welded after maintaining the press for a few minutes.

Fabrication of the On/Off System: PDMS prepolymer was spin cast on a slide glass (500 rpm, 20 s) and cured (80 °C, 2 h). Poly(styrene-*b*-butadiene-*b*-styrene) (styrene:butadiene = 3:7) was dissolved in chloroform (3 wt%) and the solution was spin cast on PDMS stamp having a width of 300 μm (3000 rpm, 1 min). And the SBS film on PDMS stamp was annealed at 150 °C for 20 min. The PDMS film with the SBS film and PDMS reservoir was bonded by oxygen plasma (Cute-B, Femto Science, Korea, 50 W for 30 s).

Release Test in a PBS Buffer Solution: An aqueous solution of rhodamine B (0.01 wt%) was injected in the spherical reservoir through an injection needle. The patch was soaked in a 3 mL PBS buffer solution and maintained for 10 min, after which a bending motion was applied. The bent state was maintained for 1 min in each bending event. For reliable bending deformation, arc shape templates having different curvatures (r = 45, 27, and 19 mm) were used, and the patch was gently attached on the template to prevent its local deformation. The buffer solution containing the released rhodamine B was thoroughly collected and fresh PBS buffer solution (3 mL) was added after every bending event to obtain accurate results for each bending event. After finishing the whole set of release tests, the patch was cut into small pieces and the residual rhodamine B in the reservoir was dissolved in another fresh 3 mL buffer solution. The concentration of rhodamine B in the collected solutions was measured by a multimode microplate reader (Synergy TM

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H4, BioTek). Three samples were compared for each bending motion studied.

FEM Simulations: A full 3D bending simulation of the PDMS patch was conducted using the commercial FEM package "HyperWorks 12.0." A 4-point bending method was applied to deform the patch until it was bent up to a desired radius (r = 45, 33, 27, 22, and 19 mm). The constitutive relation was constructed by fitting the tensile test result of a cured PDMS at the same condition. An incompressible second-order Ogden model hyperelastic form was used as shown in Equation (2) as follows

$$\sigma = \sum_{i=1}^{2} \frac{\mu_i \left(\lambda^{\alpha_i} - \lambda^{-\frac{\alpha_i}{2}} \right)}{\lambda} \tag{2}$$

where λ is the principal stretch along the loading direction. Isotropic material constants are obtained as α_1 = 2.7727 e^{-3}, α_2 = 21.732, μ_1 = 892.18 MPa, μ_2 = 4.2796 e^{-5} MPa (i = 1, 2 in the second-order Ogden form).[34] During the bending simulations, the left end of the patch was completely fixed, and the other end was free to move along the length direction of the patch. A total of 600 000 tetragonal elements were used and the mesh was gradually refined near the surface of the reservoir. A spherical hollow reservoir with a 1 mm radius was centered at 2.02 mm from the patch bottom. The channel dimension was set to be f_{ch} = 2%.

The patch in the simulation was intentionally made ten times longer in length than the real patch so that the central region between the two inner loading points was as wide as possible. According to Saint-Venant's principle, this configuration can avoid any undesirable effect of locally concentrated point force on the deformation of the reservoir. Once the patch structure was bent with a particular radius, the deformed reservoir was inscribed with a large number of tetragonal elements constructed from the reservoir surface nodes, and the volume of the deformed reservoir was approximated as the volume of total tetragonal elements, which was later used to calculate the volume change of the reservoir.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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