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Auto-adhesive transdermal drug delivery patches using beetle inspired micropillar structures†

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The patch described in this paper combines the principles of wet adhesion, which is a widely adopted biological adhesion system in nature, with transdermal drug delivery. A biologically inspired micropillar patch was fabricated that is self-adhesive, reusable, and can sustain a controlled drug release. We successfully preloaded the commercial non-steroidal anti-inflammatory generic drug unguents indomethacin, ketoprofen, diclofenac sodium and etofenamate into a polydimethylsiloxane elastomeric matrix and fabricated drug-containing micropillar patches. When examining the drug release kinetics and friction of the patches, we observed that these drug unguents can be released calculably and regularly for several days. Additionally, the drug unguents released from the patch to its attached surface are critical to increase the strength of the patch's adhesion, which is based on capillary attractive forces and is inspired by beetle feet. Here, we create a novel system combining biomimetics and drug delivery that can be modified for use across the biomedical and engineering spectra. *Motivation*: the objective of the present study was to characterize a micropillar PDMS patch that was inspired by a beetle's wet adhesion as a platform for conducting *in vitro* release studies. Commercially available non-steroid anti-inflammatory drugs (NSAIDs) were used as the model drugs for our delivery systems. An emphasis was put on quantitatively evaluating the drug release and friction manifestation of these patches.

1. Introduction

Transdermal drug delivery (TDD) is an attractive method, offering opportunities to address the low bioavailability of many oral drugs and to avoid the pain and inconvenience of intravenous (i.v.) drug administration.[1] In practice, the advantages of transdermal administration include high patient compatibility with the treatment, the ability to discontinue the treatment at any time, a controlled rate of drug delivery to the patient, a fixed plasma drug level and the elimination of the hepatic first-pass effect.[2] TDD systems currently include several types of transdermal patches, and at least three generations of manufacture.[3] However, all of these transdermal patches contain an adhesive layer, need firm contact with the skin, and ensure that the drugs access the systemic circulation at a controlled release rate. Here, we propose that in cases of a self-adhesive patch matrix, a special adhesive layer is not needed. Hence, a bandage inspired by insects' feet is a possible matrix upon which to construct an auto-adhesion TDD composite (Chart 1).

The adhesion that occurs on the feet of some insects and animals has been attributed to a combination of molecular interactions and secretion-mediated capillary attractive forces.[4] Because some insects produce secretory fluids in the contact area[5] but others do not (spiders and geckos),[6] sciec3tb20735h-ttists can expect that different basic physical forces contribute to the overall adhesion. After studying these adhesive systems, many scientists have mimicked water beetle feet,[7] tree frog toes,[8] and gecko toes[9] when engineering materials for technological applications. The advances in understanding such mechanisms are relatively recent. We are most interested in the

Chart 1

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development of wet adhesion for medical purposes, including recent research showing that an endoscopic video capsule can stop and anchor itself within the internal intestinal surface due to an enhanced adhesive and frictional micropillar array.[10] Additionally, a treatment tape for surgical and traumatic wounds was designed with nanoscale pillar arrays, which can enhance the properties of an internal tissue.[11] It seems that wet adhesion has a broader biomedical engineering utility than dry adhesion. Recently, dry adhesion nano- or micro-fiber arrays were coated with adhesive proteins secreted by marine animals to construct friction enhancing wet elastomeric adhesive tapes.[10,12] Consequently, a bandage inspired by gecko feet was constructed and suggested as an eventual replacement to suturing.[13] However, there has been no discussion of their use in TDD until now. In this manuscript, we study the effects on the adhesion force of a wet adhesion system when preloading a drug into the elastomeric matrix. The goal of this study is to improve the design of micromanipulation systems by incorporating capillary forces, an idea learned from bio-mimicking.

Because elastomers are commercial polymers that offer unique biocompatibility characteristics and are not biodegradable, they are widely used in biomaterials,[14] particularly in medical devices for drug delivery[15] or drug release.[16] Among medical grade silicones, PDMS (polydimethylsiloxane) and PDMS-based elastomers not only satisfy the above standards but can also be used in skin topical applications and long term implants.[17] The literature indicates that PDMS can release low molecular weight siloxane (an oil),[18] a homogeneous lubricious alcohol,[19] or lignocaine.[20] Furthermore, PDMS/silicone resin networks, matrices made of silicone pressure-sensitive adhesives, are used in numerous TDD systems to affix the drug device to the skin.[21] More importantly, PDMS has been successful as a reusable micro-scale mold to fabricate microneedles.[22] Most of the adhesion systems described above that were made of nano- or micro-fiber arrays were constructed from PDMS or PDMS-based elastomers. Overall, the properties of PDMS are suitable for the fabrication of nano- or micro-arrays, as well as for the formation of a drug-releasing matrix. Thus, we chose PDMS as the matrix material to fabricate our bio-inspired self-adhesive TDD tape.

2. Experimental

2.1 Materials

2.1.1 Silicone matrix. Polydimethylsiloxane (PDMS, Dow Corning Inc., Midland, MI, USA), a soft elastomer, was selected as the material used in the micro-pattern because PDMS can be easily fabricated and is biocompatible.[23] It is a room-temperature vulcanizable (RTV) silicone consisting of two liquids, A and B, which are packaged separately. The first liquid contains the monomer and the inhibitor, and the second contains the crosslinking promoting agent (platinum salt).[24] Here, we prepared three raw elastomers made of three types of silicone grade PDMS, Silastic® T-4, Sylgard® 184, and Dow Corning® SE1740. The patches were fabricated under different preparation conditions.[25]

2.1.2 Preparation of micropillar patches. As seen in Fig. 1, the two components of the silicone are mixed together (at a ratio of 10/1 monomer/catalyst, w/w) in ultrasonic baths to obtain a homogeneous, low viscosity liquid. The PDMS mixture is then poured over a mold of micro-holes with a defined geometry (hole diameter = 2 μm, height = 2 μm and period = 4 μm), degassed (10 mmHg) in a vacuum chamber for 20 min, and cured without heating. We prepared the patches containing the drug (or oil) using the same procedure, by mixing the drugs with the A and B liquids (each patch included 1 g or 1 O.D. of drug). Finally, the PDMS patch was peeled away from the mold used to fabricate micropillars. A representative sample of the resulting molded micropillars is also shown in Fig. 2. The transparent elastomeric tape was identified by lighting it with a laser point; as shown in Fig. 2(a), the regular pattern of laser-induced bright spots that mimicked the micropillar spacing of the tape was evident once the curing and casting processes were successful. A scanning electron microscopy micrograph was used to check the structure and regularity of the pillars on the patch, as shown in Fig. 2(b) and (c).

Consider the mechanical stability and surface energy of the micropillar patch. Long fibers tend to be mechanically unstable and may collapse as a consequence of their own weight or cluster if the adhesive forces between the contact tips become

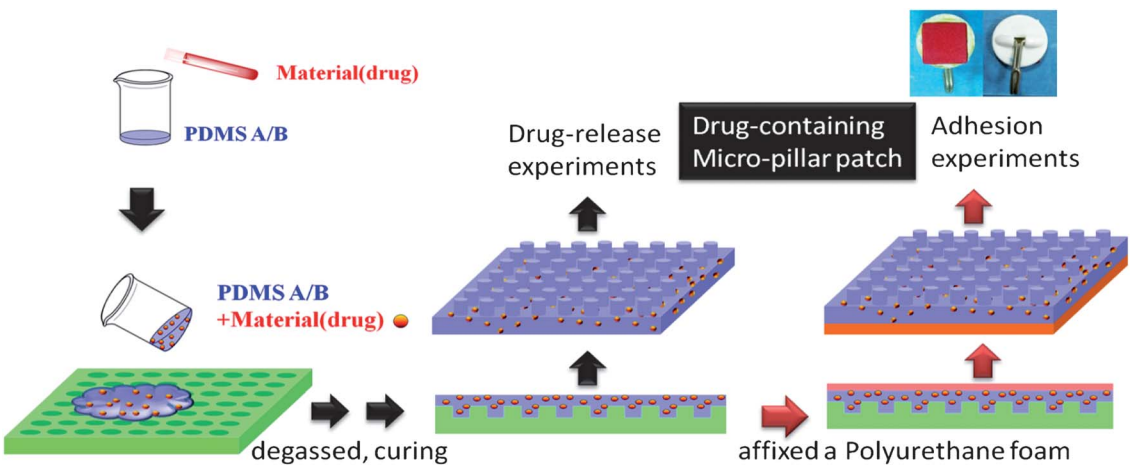

Fig. 1 A flow chart showing the preparation of the drug-containing micropillar patches.

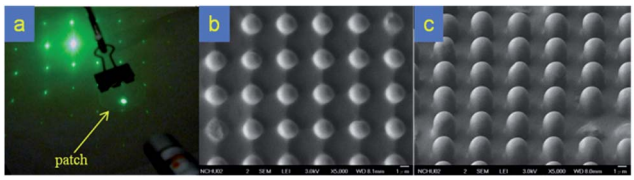

Fig. 2 (a) Identification of the PDMS micropillar array using a laser point. (b) A scanning electron microscopy micrograph of the patch shown in (a), with an approximate diameter of 2 μm, an approximate height of 2 μm and a pillar spacing of 4 μm (center to center). (c) The same array as that shown in (b), but at a 45° angle view.

stronger than the forces required for bending.[26] That is, bending or condensation easily occurs around pillars with a too small radius or around those that are too long or too close. Hence, an adhesive structure consisting of micro- or nano-fibers with radii, lengths and inter-fiber distances (density) should follow the criteria of "adhesion design maps", which are based on the comprehensive evaluation of the fiber fracture, ideal contact strength, fiber condensation and fiber adaptability.[27] Moreover, thinking about the wet adhesion system, whether coating or preloading, the pillars will become heavy and the inter-fiber distance is shortened. Larger spacing and shorter diameter are favourable to prevent the fiber or pillar from condensation. Following these considerations above, we design our micropillar tape at this stage.

2.1.3 Therapeutic agent. Hydrocortisone and (−)-nicotine were obtained from Acros Organics Co. Thiamine hydrochloride was purchased from Sigma, and methyl salicylate was obtained from Alfa Aesar. The NSAIDs used included etofenamate, containing Teiria gel (5% w/w, U-Chiu Pharmaceutical Co., Taiwan); diclofenac sodium, containing Canfol gel (1% w/w, Fu-Yuan Chemical & Pharmaceutical Co., Ltd, Taiwan); ketoprofen, containing Fastum gel (2.5% w/w, A. Menarini, Italy); indomethacin, containing anodyne solution (1% g ml^{-1}, Root Chemical Pharmacy Co. Ltd, Taiwan); methyl salicylate, containing mentholatum deep heating rub (TTY Biopharm. Co., Ltd, Taiwan); and dimethyl silicone oil (KF-96 1000 c.s., Shin-Etsu).

2.2 Measurements

2.2.1 Adhesion experiments. Adhesion experiments were performed to determine the pull-off phenomena of removing each strip of the micropillar tape from glass. Buckets containing various weights of water were hung from a patch adhered to glass. The friction results were described by either tensile force testing (a bucket hung from a patch with its glass mounted on the ceiling) or shear force testing (a bucket hung from a patch with its glass mounted on the wall). To hang a bucket, polyurethane foam was affixed to the back of a patch, as shown in Fig. 1, and then a hook was gummed to the foam.

2.2.2 Controlled release of the drug. The fabricated silicone patches were attached to a piece of smooth glass, which was removed once a day (from days 1 to 8). The amount of the drug released was determined by measuring the absorption signal of the reagents remaining in the tapes. The absorption of the tape was measured *via* UV spectroscopy (Thermo Genesys 6 UV-visible spectrophotometer). To create control curves for comparison, the basic absorption and emission spectra of the generic drug and ointment mixtures were collected and are shown in Fig. S1.†

3. Results and discussion

3.1 Fabrication of the PDMS micropillar patches

At first, it is necessary to evaluate the mold-casting and drug-releasing abilities of the fabricated micropillar patches. After fabricating as described in the Experimental, the produced tape made using Silastic® T-4 was the hardest of the three tapes, while that made using Dow Corning® SE1740 was the stickiest and the most elastic. These three silicone grade PDMS elastomers were used in this work to determine the optimal balance between the drug release rate and the friction of wet adhesion tapes. In fact, an earlier report showed that dimethyl silicone oil can be released from PDMS.[18] Thus, in the first stage we incorporate dimethyl silicone oil into the PDMS elastomers listed above before curing the patch, qualitatively observing the oil release from the patch. In the meantime, in order to better observe the drug releasing conditions, we quantitatively measured the kinetic release of the oil by dissolving a trace of fluorophore powder in the silicone oil. Consequently, the fluorescence emission signal of the fluorophore-inclusive fluorescent oil was the criterion to numerically evaluate the controlled drug release. After an initial screening, we found that all three micropillar PDMS tapes could constantly release the silicone oil, but only the tapes molded of Sylgard® 184 and Dow Corning® SE1740 PDMS released the fluorophore (Fig. S2†). The fluorophore was retained in the matrix of the Silastic® T-4 tape. Thus, for a solute-solvent mixed drug system, Silastic® T-4 tape is not suitable to be a containing matrix because it only releases the solvent, not the solute. Additionally, Dow Corning® SE1740 PDMS tape is difficult to peel from the mold, though it can release a powdered fluorophore without requiring a solvent like silicone oil (data not shown). In summary, the micropillar tape made from Sylgard® 184 PDMS is the most suitable matrix to contain a drug such as the ointment mixtures used in this paper (described in the Materials section).

3.2 The wet adhesion of micropillar patches containing silicone oil

We are interested in not only the release of oil from the manufactured tapes but also the change in the wet adhesion of the micropillar tape containing oil. Adhesion experiments were performed on Sylgard® 184 micropillar tapes, both unloaded (termed dry adhesion) and loaded with dimethyl silicone oil (wet adhesion). The peel-off force was easily determined for each tape by tensile force testing (in which the bucket hangs downward when the glass is affixed to the ceiling) and shear force testing (in which the bucket hangs to the side of the patch when the glass is affixed on the wall, as shown in the insets of Fig. 3). Various weights of water-containing bottles were used to reach the failure point, and the mean force values are plotted in

Fig. 3 as a function of the loading percentage of oil. The experimental results indicate that a certain ratio of silicone oil can result in an increased frictional force. In the side hanging case, the shear force reaches a maximum of 5 N cm^{-2} when the dose percentage of the silicone oil is 5%. A maximum tensile force of 9.6 N cm^{-2} is reached in the hanging case when 15% oil is used. Both of these forces are larger than those obtained with only the dry adhesive patches. However, the frictional forces decrease when silicone oil preload percentages of above 5% or 15% are used in the hanging and side hanging micropillar patches, respectively. We propose that an excess amount of oil will fill the space between the pillars and destroy the van der Waals interactions that normally aid adhesion. Furthermore, in the side hanging case, the micropillar tape containing excess oil is very easy to slide along the wall when lateral force is applied. That slide is why the wet adhesion efficiency of the side hanging tape is lower than that of the hanging tape. Nevertheless, the wet adhesion micropillar tape that is inspired by beetles was successfully fabricated to continually release a contained liquid. Following the results and discussions above, a generic drug dosage of 5% was selected to complete the following studies.

Based on the descriptions in the Introduction, there is no doubt that the friction should dramatically increase once a flat patch (non-micropillar) becomes a micropillar structure. However, the literature also mentioned that the viscosity of coating oil may affect the frictional force.[10,12] That is, we should take the viscosity effect of preloading oil into consideration. In our system, the friction of the dry flat patch is lower than 0.3 N cm^{-2}. Furthermore, the oil-preloaded flat patch never achieved twice the value of friction force, as shown in Fig. S3.† Hence, relative to the flat patch, we infer that contributions to the frictional force of the micropillar patch are predominantly from the micropillar structure, and this kind of adhesion may further increase with appropriate oil doping which is due to the capillary attractive force but not to the viscosity of the secretion (the oil released from the tape).

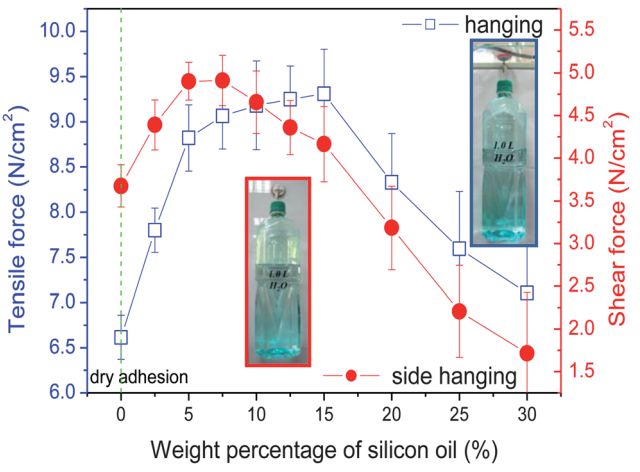

Fig. 3 The results of a friction test on the Sylgard® 184 micropillar patch with variable weight percentages of preloaded silicone oil. The tensile force test of a hanging bucket, suspended from a patch affixed to the ceiling, is shown in blue. The shear force test of a side hanging bucket, suspended from a patch affixed to the wall, is shown in red.

3.3 Release kinetics of the drug-containing micropillar patches

We wanted to evaluate whether the inclusion of reagents would interfere with the polymerization of PDMS during the micropillar patch preparation. The experimental procedures were performed as described above; generic drugs were mixed with ointments from the drugstore, and the mixture was preloaded into the PDMS solution before the silicone was cured. The preloaded drugs hydrocortisone, etofenamate, diclofenac sodium, ketoprofen, indomethacin and methyl salicylate were molded successfully into the PDMS micropillar patches, as expected. However, we found that the addition of nicotine or thiamine hydrochloride hindered PDMS polymerization, preventing the production of a flexible transparent patch. Fig. 4 illustrates the release kinetics of the generic drugs that were successfully incorporated into the Sylgard® 184 silicone elastomer.

As described above, in order to quantitatively determine the amount of drug released from the patch, we measured the intensity of the absorption signal of the drug which remained in the tape. The results show that preloaded etofenamate and diclofenac can easily be released from the PDMS patches. After 4 days of adhesion (with a new piece of glass affixed everyday), approximately 55% of the active ingredient was released. The ketoprofen-containing patch had a lower release percentage (20%), likely due to the more viscid property of the ingredient, causing larger deviation from the curve norms. Spectral detection showed that hydrocortisone and indomethacin are only marginally released from the gel, even when the monitoring period is extended to 8 days (data not shown), indicating that these drugs were contained within the patches. A significant amount of methyl salicylate was released from its patch in the very early stages; we clearly observed the absorption signal of methyl salicylate once the drug-containing patch had been cured, but the signal was completely reduced over the course of mere hours. We inferred that this initial burst effect occurred because the methyl salicylate was deposited only on the surface of the patch and was not physically incorporated into the silicone matrix. A similar phenomenon was also found in a silicone polymer matrix containing lidocaine hydrochloride in another study.[28] On the other hand, the release efficiencies between micropillar and flat patches were also checked. Based on the result from Fig. 4, the etofenamate and diclofenac preloading PDMS patches have better drug release curves than others. As observed from the flat patches under similar experimental conditions, Fig. S4† showed that only 17 and 20.5% of etofenamate and diclofenac were released after 4 days of adhesion, respectively. It is reasonable to conclude that the micropillar structure can provide a larger surface area for drug release, with respect to the flat structure.

In order to enhance the releasing efficiency without chemically modifying the PDMS structure, the addition of penetration enhancers is a common choice which should be non-immunogenic and rapidly reversible, to increase transdermal drug delivery into and through the skin.[29] There are some successful

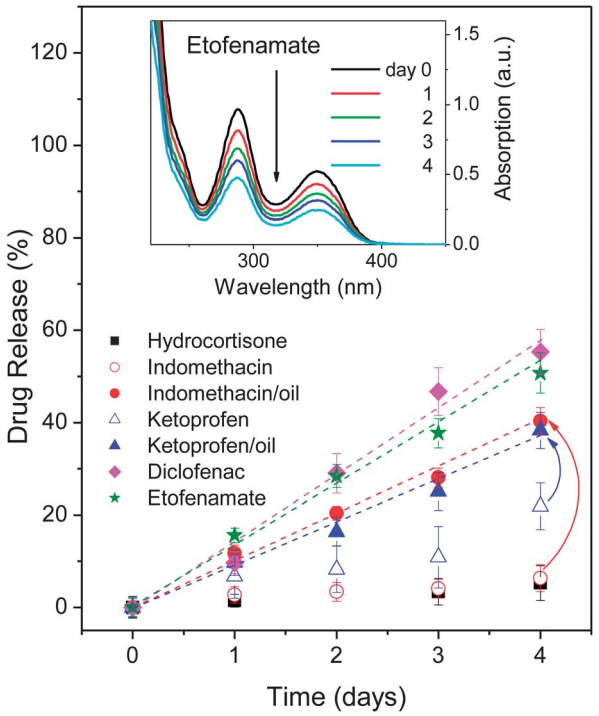

Fig. 4 The time dependent release percentages of the generic drugs hydrocortisone, etofenamate, diclofenac sodium, ketoprofen and indomethacin that were preloaded into PDMS micropillar patches. The dimethyl silicone oil doping results for the indomethacin and ketoprofen systems are also shown. A patch was attached to a glass surface, which was changed once a day. The inset shows the spectra of the etofenamate remaining in the patch over the course of the experiment.

examples of modifiers that increase the amount of drug released, such as polymer carriers[28] and excipients.[30] Although the release of the drug may be optimized, the enhancers may also affect the properties of the drug or patch. Thus, in order to improve the results shown in Fig. 4, we attempted to use dimethyl silicone oil as a carrier for hydrocortisone, indomethacin and ketoprofen. Based on the results from Fig. 4, the generic drugs with the lowest delivery rates were dissolved in silicone oil (5% total weight) before being added to the PDMS mixture. It is clear that the release slopes of the indomethacin and ketoprofen systems increased over the 4 days of the experiment, with release amounts increasing from 6 to approximately 40% and from 21 to approximately 38%, respectively. The hydrocortisone system underwent the same addition of silicone oil, but no improved release was seen. Regardless of the method used to incorporate the drug, the hydrocortisone-releasing curve remained unchanged over both short and long periods.

Fig. 4 also shows that the release kinetics of all the samples were calculable and uniform. Their spectral patterns were unchanged after 4 days, meaning that these drugs were stable in the PDMS matrix over a long period. Indeed, a plateau in the spectra was observed for all of the samples. Although the plateau effect is relative to the patch thickness, it is actually attributed to the hydrophobicity of the silicone matrix, which traps the drugs and prevents them from disseminating into the buffer solution. As illustrated in Fig. 5, a diagram of the kinetic release (the slopes of the fitting curves from Fig. 4) *versus* the lipophilicity log *P* clearly shows a linear relationship. Similar results were also observed in a diagram of the relationship between the lipophilicity log *P* and the amount of total drug released from the patches. This result indicates that the PDMS matrix is suitable for delivery of more lipophilic dugs, especially etofenamate and diclofenac. Furthermore, because hydrocortisone and methyl salicylate were not suitable for a Sylgard® 184 PDMS matrix, and nicotine and thiamine hydrochloride disrupted the polymerization of the PDMS elastomer, we concluded that NSAIDs would be suitable drugs for a multi-day release from a beetle-inspired micropillar PDMS medical device.

As an additional consideration, we found that pure chemicals ketoprofen, indomethacin and diclofenac sodium were solid powders at room temperature, while etofenamate was liquid. On the other hand, in the generic drug ingredients (containing a drug solute and a solvent or polymer carrier) we investigated in this study, the solvent could be alcohol, silicone oil, Vaseline (petrolatum-based) or even some L-menthols. In most cases, these solvents were mixed with each other and used to manufacture formulations. Hence, in our system, it is very possible that the solvents of ingredients evaporated during the curing procedure, which may reduce the efficiency of drug releasing from the patch. To conclude the lipophilicity, solvent evaporation and physical state of the compound, these factors by themselves may be the reasons for different releasing efficiencies between these NSAIDs and the possible reasons why the etofenamate and diclofenac can release from patches well without adding a solubilizing agent (dimethyl silicon oil). Nevertheless, from our results, the important message is that a commercial generic NSAID drug mixture can be successfully doped into a PDMS matrix to construct a biomimetic TDD system.

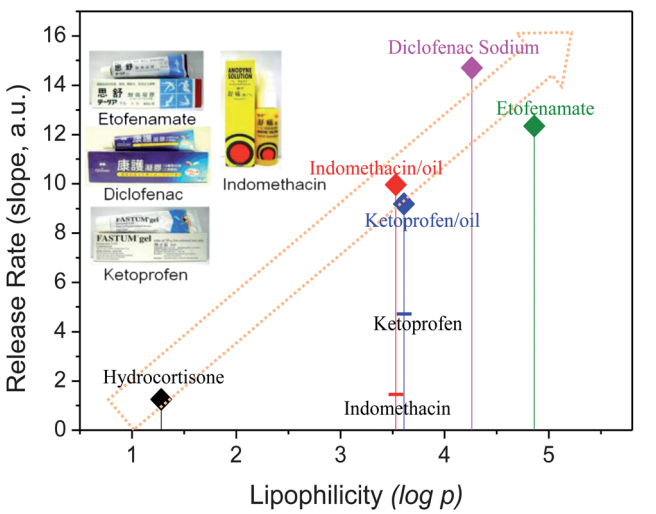

Fig. 5 A diagram of the relationship between the lipophilicity log *P* of a drug and its kinetic release (the slopes of the fitting curves from (b)). The dimethyl silicone oil doping results for the indomethacin and ketoprofen systems are also shown.

3.4 Wet adhesion or friction of the drug-containing micropillar patches

Adhesion experiments similar to those described in Fig. 3 were performed for wet adhesion PDMS micropillar patches that were preloaded with a drug. If the drug released from the TDD system can be made to mimic the secretions seen in the feet of insects and animals, wet adhesion, which can be attributed to capillary attractive forces, will be stronger than dry adhesion. As expected, the experimental results shown in Fig. 6 indicate that the inclusion of a 5% dose of commercial generic NSAIDs resulted in an increased adhesion force, whether the measurement was tensile or shear. However, we also observed that the adhesive strengths of all the patches decreased with time. The decay of the control patch's dry adhesive ability is likely due to a degradation of the pillar structures on the polymer surface with repeated use. This phenomenon also occurred in the patches preloaded with a drug and was particularly serious in the shear force measurement.

Furthermore, the more drug that is released from a patch, the more closely the experimental patch resembles the dry adhesion control due to a lessening of the capillary attractive forces. Additionally, it is possible that the released drug will also fill the space between the pillars where the patch is not in contact with the glass. As a result, the excess amount of oil or liquid drug could destroy the van der Waals interactions, as described in Fig. 3. As can be seen in Fig. 6, the better drug releasing patches, such as the etofenamate and diclofenac systems, show the adhesion decays more quickly than the other systems. On the other hand, as mentioned above, ketoprofen is the stickiest of these drug ingredients. Thus, the ketoprofen system is the most adhesive patch and it maintains its adhesion with less apparent decay. Nevertheless, these wet adhesion results illustrate that the preloaded patches have higher adhesion strengths than do the unloaded PDMS patches in both tensile and shear adhesions, even though their adhesions decay with multiple uses.

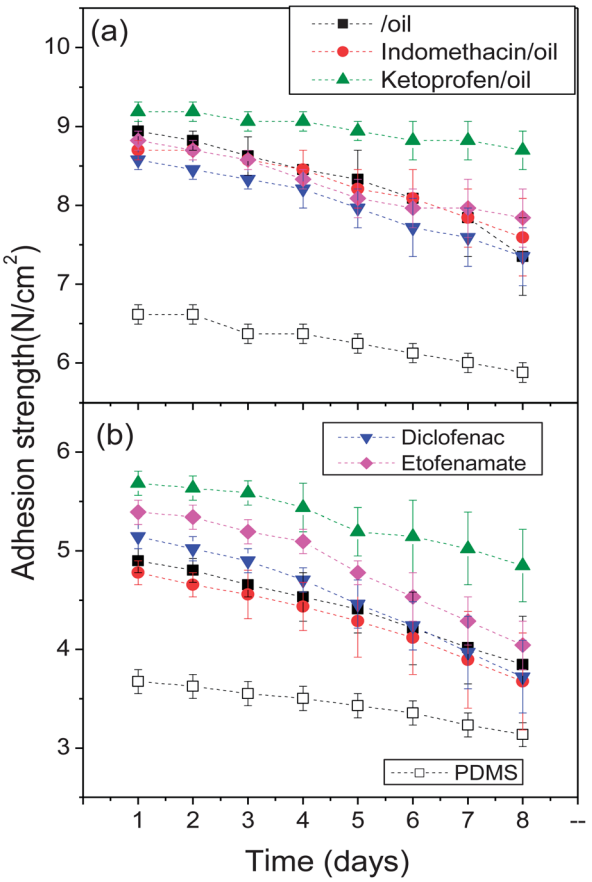

Fig. 6 The time dependent friction tests of the dimethyl silicone oil and the generic drugs (etofenamate, diclofenac, ketoprofen and indomethacin) that were preloaded into the PDMS micropillar patches. These wet adhesion experiments are compared with the control unloaded micropillar patch (dry adhesion). (a) The tensile force test, using a hanging bucket. (b) The shear force test, using a side hanging bucket. The patch was attached to a glass surface that was changed once per day.

3.5 Predicting the skin application

The optimal drugs found in this study for inclusion into our designed PDMS matrix, to be released over a period of several days, were etofenamate and diclofenac. Indeed, this device could promote the release of these therapeutic molecules when the device is attached to the skin, which can absorb a drug stage by stage. Once we determined that our system could be used as a TDD system, we attached the NSAID-containing micropillar patches to oil-blotting paper (a special oil absorbing paper often used on the face), instead of glass, to mimic the effects of the TDD on the skin and reevaluate its release kinetics. As shown in Fig. 7, approximately 52% (a 12% increase), 48% (a 10% increase), 68% (a 13% increase) and 65% (a 15% increase) of the total contained drug was released from the indomethacin, ketoprofen, diclofenac and etofenamate systems, respectively. Both the amounts and release rates of the NSAIDs delivered in this method were apparently increased as shown in Fig. 3. Here, we also observed the plateaus in the curves, which occurred early; the increasing release rates for these drugs were identical to those previously described. Therefore, we conclude that this phenomenon is caused by the drug concentration gradient, which is more pronounced between the oil-blotting paper and the patch than it was with the glass.

It is known that the oral NSAIDs can inhibit cyclooxygenase isoenzymes (COX-1 and COX-2) and result in reduced synthesis of prostaglandins,[31] provide analgesia and relief from inflammation, are used to reduce the concentration of prostaglandins at the site of injury resulting in decreased pain and inflammation.[32] However, NSAIDs can also lead to an increased risk of gastrointestinal[33] and cardiovascular adverse events.[34] The superiorities of TDD, as described in the Introduction section, can avoid the side effects of NSAIDs. TDD administered NSAIDs penetrate slowly and in small quantities into the systemic circulation. These approaches also prevent high local drug levels in the alimentary tract and direct toxicity of NSAIDs with reduction in the total daily dosage of systems, especially in long term treatment.[35] Finally, TDD applied NSAIDs have a superior safety profile to oral formulations.

Here, in our system, the results in Fig. 4 and 7 indicate that the absorption capability of a substance (*e.g.*, skin) can affect

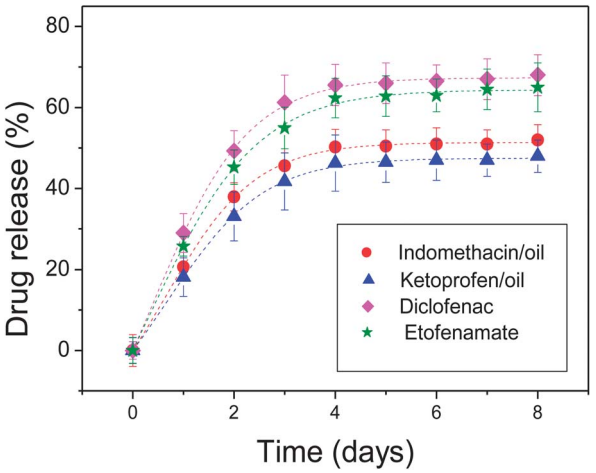

Fig. 7 The time dependent release percentages of the generic drugs etofenamate and diclofenac sodium, as well as oil-doped ketoprofen and indomethacin, which were preloaded into PDMS micropillar patches. The patches were attached to a surface of oil-blotting paper, which was changed once per day.

the drug release of our patch. That is, the properties of the substance to which the patch is attached may influence the quantity and rate of drug release. Thus, in our micropillar wet-adhesion patches, we not only retained the superiorities of TDD but also promoted the applications of TDD. Once these solvents or polymer drug carriers are incorporated into a TDD system, they will be suitable wet-adhesion patches, constructed based on the idea of capillary attractive forces that are mediated by secretions. In our study, the commercial ingredients etofenamate, diclofenac, ketoprofen and indomethacin were successful examples. This issue can be commercialized immediately with low-cost unguents (commodities) and simple manufacture procedures, especially in etofenamate and diclofenac cases. Moreover, these successful drug-containing micropillar patches can be removed and reused several times.

4. Conclusions

In this manuscript, we constructed a new drug delivery method that combined biologically inspired wet adhesion with transdermal drug delivery. PDMS, often used as the matrix of a TDD system, was easily molded to become a micropillar patch. Here, we successfully preloaded commercial generic NSAIDs into the Sylgard® 184 PDMS elastomer and made the silicone into drug-containing TDD micropillar patches. The distinguishing features of the manufactured patches are described below. (1) The drug is released from the patch in a controlled manner that is both quantitative and uniform. (2) The adhesion strength is increased due to the drug unguents released from the patch, based on the designed capillary attractive forces that were inspired by beetle feet. (3) The patch is self-adhesive and can be removed and reused several times. (4) All of the raw materials used are biocompatible, cheap and safe. We believe that this platform can be broadened to other generic drugs once the polymer matrix is modified appropriately.

Acknowledgements

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