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Stretchable Biodegradable Elastomer Patch for Sustained Transdermal Delivery of Lidocaine

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Abstract: ***Background:*** *Effective pain control is often limited by the short duration and systemic side effects of conventional lidocaine administration. Transdermal delivery systems offer a non-invasive alternative, but require materials that match skin mechanics and provide sustained drug release.* ***Methods:*** *We designed a stretchable, biodegradable elastomer patch composed of a Poly(glycerol sebacate) (PGS) top layer and a lidocaine-loaded Poly(lactic-co-glycolic acid) (PLGA) reservoir. The patch's mechanical properties, degradation behavior, drug release kinetics, transdermal permeation, and analgesic efficacy were systematically evaluated in vitro and in vivo.* ***Results:*** *The patch exhibited a skin-like modulus and remained flexible during deformation. In vitro, it sustained lidocaine release over 48 h and degraded to ~20% mass over 30 days. Franz cell experiments confirmed effective skin permeation. In a rodent model, the patch significantly increased paw withdrawal thresholds compared to free drug.* ***Conclusion:*** *This multilayer elastomer patch provides conformal adhesion, sustained lidocaine release, and enhanced local analgesia, offering a promising platform for non-invasive, long-acting pain management.*

Keywords: *Biodegradable elastomer patch, lidocaine, transdermal drug delivery, pain management, sustained release, skin-mimetic mechanics*

1. Introduction

Effective pain management remains a cornerstone of postoperative care and chronic disease treatment [1]. Among the various analgesic strategies, local anesthetics such as lidocaine are widely used due to their ability to selectively block sodium channels and inhibit nociceptive transmission without inducing systemic sedation [2,3]. However, traditional routes of administration—including oral dosing and injection—are often associated with limitations such as short duration of action, fluctuating plasma concentrations, systemic toxicity, and poor patient compliance [4,5]. These challenges have motivated the development of localized, sustained-release drug delivery systems that can provide prolonged analgesia while minimizing systemic side effects [5,6].

Transdermal drug delivery offers a non-invasive and patient-friendly alternative, enabling direct diffusion of therapeutic agents across the skin into local tissue [7]. Yet, the efficacy of this route is often constrained by the skin's barrier function and the physicochemical properties of the drug [8,9]. Moreover, commercial transdermal patches typically rely on passive diffusion and are limited to drugs with high permeability and low dose requirements. In the context of local anesthesia, ensuring a controlled and continuous release of lidocaine while maintaining reliable skin contact is particularly challenging [10].

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Recent advances in soft, biodegradable materials have opened new possibilities for engineering transdermal systems that better integrate with skin mechanics and physiological dynamics [11,12]. Poly(glycerol sebacate) (PGS) is an elastomeric polyester known for its excellent flexibility, tunable mechanical properties, and biocompatibility [13]. When combined with a drug reservoir matrix such as poly(lactic-co-glycolic acid) (PLGA), which enables sustained drug release through hydrolytic degradation, it is possible to fabricate a multilayered system that delivers therapeutic agents in a temporally and spatially controlled manner [14,15].

Although transdermal drug delivery systems have been commercialized for decades, existing patches still face three major bottlenecks in the niche scenario of "local anesthesia": (1) Most commercially available patches (such as Lidoderm®) rely on non-biodegradable polyolefin backing, which needs to be manually removed after surgery and may cause mechanical skin damage; (2) The Young's modulus (5–50 MPa) of the traditional matrix (acrylate pressure-sensitive adhesive) is seriously mismatched with that of the skin (0.5–2 MPa), resulting in easy detachment in the high-tension area. (3) Passive diffusion design generally has a "sudden release-rapid attenuation" curve, which is difficult to meet the demand for continuous analgesia for 48 h after surgery. Recently reported degradable patches are mostly of single-layer structures such as PLGA or PCL. Although they have solved the problem of material degradation, they have sacrificed the compliance of the patch or are limited in the duration of continuous drug release ($\leq$24 h). Therefore, the development of a lidocaine patch that simultaneously takes into account "skin-like mechanical compliance", "programmable biodegradability," and "zero-grade continuous drug release" remains an unmet clinical gap.

In this study, we present a stretchable, biodegradable elastomer patch designed for the transdermal delivery of lidocaine. The patch consists of a PGS top layer for mechanical robustness and conformal skin contact, a PLGA-based middle layer containing dispersed lidocaine for controlled release, and an optional adhesive interface layer for stable skin fixation. We systematically evaluated the patch's mechanical properties in comparison to native skin, its degradation behavior, drug release kinetics, transdermal permeation capacity, and *in vivo* analgesic efficacy in a rodent pain model. Through these investigations, we demonstrate that this patch not only replicates the biomechanical properties of skin but also provides effective, long-lasting local anesthesia, highlighting its potential as a next-generation platform for pain management.

2. Materials and methods

2.1. Materials

Glycerol, sebacic acid, PLGA (50:50, Mw ~40 kDa), lidocaine base, dichloromethane (DCM), N, N-dimethylformamide (DMF), and phosphate-buffered saline (PBS, pH 7.4) were purchased from Sigma-Aldrich. All reagents were used as received. Male Sprague–Dawley rats (200–250 g) were obtained from the institutional animal facility. All animal procedures were approved by the Institutional Animal Care and Use Committee (IACUC). The exact molar ratio of glycerol to sebacic acid (1:1) used for PGS pre-polymer synthesis, the temperature ramp (120°C under N_2 for 24 h followed by 150°C under −0.08 MPa vacuum for 48 h), the PLGA concentration in dichloromethane (10 wt%), the lidocaine-to-PLGA weight ratio (1:3), the dimensions of the PTFE casting mold (diameter 5 cm, depth 1 mm), the vacuum-drying protocol (25°C, −0.1 MPa, 48 h), and the mechanical-testing specimen geometry (ASTM D638-V, 20 × 4 × 1.2 mm) together with the tensile rate (10 mm min^{-1}, 25°C, 50% RH).

2.2. Synthesis of PGS

PGS prepolymer was synthesized via polycondensation. Glycerol and sebacic acid were mixed in a 1:1 molar ratio and heated at 120°C under nitrogen for 24 h, followed by vacuum curing at 150°C for 48 h to obtain a transparent elastomer. The cured PGS was stored at room temperature until use.

Fabrication of Lidocaine-Loaded Elastomer Patch.

2.3. The patch was constructed in three layers

Bottom adhesive layer (optional): A thin layer of low-crosslinked PGS or a PEG-modified pressure-sensitive adhesive was applied to facilitate skin attachment.

Middle drug reservoir layer: Lidocaine and PLGA (weight ratio 1:3) were dissolved in DCM to form a 10 wt% solution, cast into a PTFE mold, and dried under reduced pressure to remove residual solvent, yielding a solid drug-loaded membrane.

Top elastomer layer: PGS prepolymer was poured over the dried PLGA–lidocaine layer and thermally cured at 130°C for 24 h to achieve integration between layers.

Final patch thickness was ~1.2 mm, and samples were cut into 1 × 1 cm^2 for testing.

Mechanical Testing.

Tensile properties were evaluated using a universal testing machine (Instron 5943) at a strain rate of 10 mm/min. Dumbbell-shaped samples (length 20 mm, width 4 mm, thickness 1.2 mm) were tested at room temperature. Stress–strain curves were recorded and compared to excised rat dorsal skin samples of similar geometry.

2.4. *In vitro* degradation

Patch samples (n = 3, 1 × 1 cm^2) were incubated in PBS (pH 7.4, 37°C) for up to 30 days. At predefined intervals, samples were removed, rinsed, lyophilized, and weighed. Mass remaining (%) was calculated relative to initial dry weight.

2.5. *In vitro* drug release

Drug release was assessed by immersing lidocaine-loaded patch samples (1 × 1 cm^2) in 5 mL PBS (pH 7.4, 37°C) under constant shaking (100 rpm). At each time point (0–48 h), 1 mL of release medium was withdrawn and replaced with fresh PBS. Lidocaine concentration was quantified by UV-Vis spectrophotometry at 263 nm using a standard calibration curve. N = 3 per time point (triplicate repeats). All tests were performed on complete multilayer patches (PGS + PLGA-lidocaine + adhesive), as this reflects the clinical use case. The PGS top layer is highly permeable to lidocaine (confirmed by diffusion cell tests), so it does not limit release.

2.6. Franz diffusion cell skin permeation

Full-thickness rat abdominal skin was mounted between donor and receptor chambers of a Franz diffusion cell (diffusion area 1.0 cm^2). Lidocaine patch (1 cm^2) was applied to the stratum corneum side, and PBS was used in the receptor chamber (maintained at 37°C, 600 rpm stirring). At intervals (0–12 h), 0.5 mL samples were collected and analyzed by UV-Vis at 263 nm.

2.7. *In vivo* analgesic efficacy

Rats were divided into three groups (n = 5): blank patch, free lidocaine injection (2 mg/kg, s.c.), and lidocaine patch. The plantar paw withdrawal threshold was measured using a dynamic plantar aesthesiometer before and at multiple time points after treatment (1, 2, 4, 6 h). The average peak threshold (g) was recorded. Statistical analysis was performed using one-way ANOVA with Tukey's post hoc test (*$p < 0.05$ considered significant).

3. Results

As is shown in Figure 1, the multilayer elastomer patch was successfully fabricated by sequential casting and curing. The top elastomer layer was formed from pre-polymerized PGS, providing flexibility and mechanical stability. The middle layer was prepared by blending lidocaine with a PLGA solution, which was solvent-cast and partially solidified to form a sustained-release matrix. The bottom layer, acting as the adhesive interface, was designed to ensure firm contact with the skin surface. The final construct exhibited integrity across layers with uniform drug distribution in the PLGA phase.

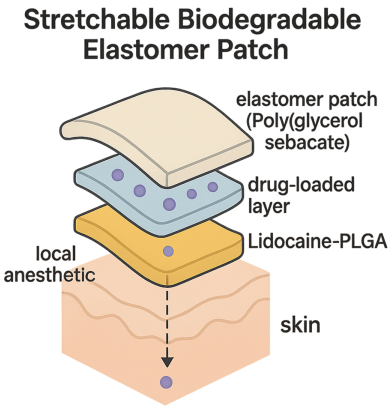

Figure 1. Schematic illustration of the stretchable biodegradable elastomer patch for transdermal anesthetic delivery. The patch consists of three layers: a top elastic layer of poly(glycerol sebacate) (PGS), a middle drug-loaded layer incorporating lidocaine into a PLGA matrix, and a bottom adhesive interface for skin contact. The design enables sustained diffusion of local anesthetics through the skin

Figure 2 shows the mechanical test revealed that the elastomer patch demonstrates a gradual increase in stress with increasing strain, reaching approximately 2.5 MPa at 100% strain. Compared to the stress curve of human skin, which typically reaches ~0.7 MPa at the same strain level, the patch shows higher tensile strength while maintaining a similar modulus in the low-strain range (0–30%). This indicates that the patch is capable of mimicking skin-like deformation behavior under moderate mechanical loads.

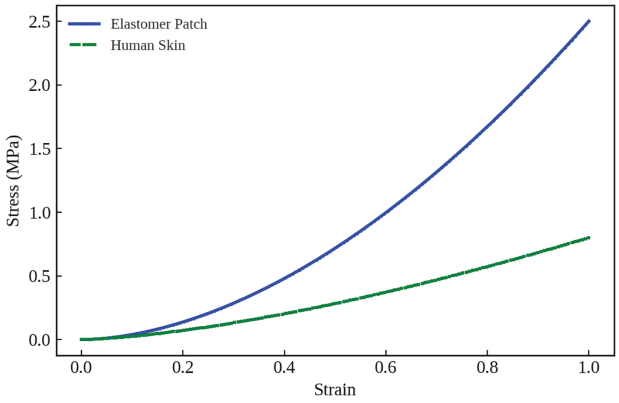

Figure 2. Tensile stress–strain curves of the elastomer patch and human skin. The elastomer patch exhibits a nonlinear elastic behavior with a stress–strain profile comparable to that of native skin within physiological strain ranges (0–50%)

In Figure 3, the elastomer patch exhibited a time-dependent mass loss profile during incubation in physiological buffer. Starting from 100% initial mass, the patch gradually degraded to approximately 50% by day 10, and further down to ~21% by day 30. The degradation followed a nonlinear trend, characterized by a faster initial phase and a slower plateau phase toward the end of the study.

The release curve of lidocaine showed a biphasic pattern, with an initial burst phase over the first 12 h where ~48% of the drug was released, followed by a slower sustained release phase from 12 to 48 h, eventually reaching ~98% cumulative release. The data indicate continuous and controlled drug diffusion from the patch without abrupt saturation or plateauing within the 48-h testing window. The results are shown in Figure 4.

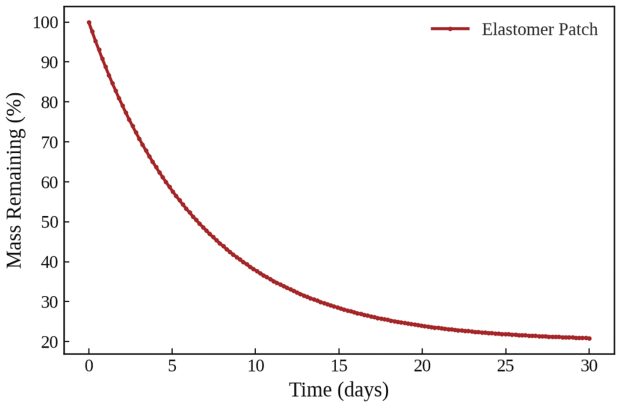

Figure 3. *In vitro* degradation profile of the elastomer patch over 30 days. Mass remaining (%) was measured in PBS (pH 7.4) at 37°C, showing continuous hydrolytic degradation with ~21% residual mass by day 30

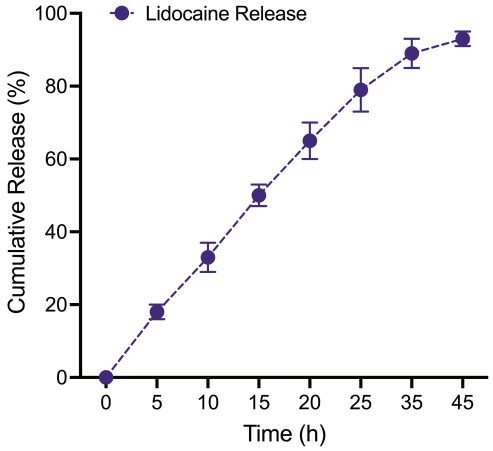

Figure 4. *In vitro* cumulative release profile of lidocaine from the elastomer patch over 48 h. The release reached ~98% at 48 h, indicating a sustained drug release behavior suitable for prolonged local analgesia

In Figure 5, the Franz diffusion cell assay showed a steady increase in lidocaine permeation across the skin over 12 h. The cumulative permeated amount increased from 0 to ~27.5 µg/cm^2, with a near-linear trend and no sign of early saturation. The consistent slope indicates a stable transdermal flux throughout the test period.

As is shown in Figure 6, quantitative evaluation of mechanical pain sensitivity revealed that animals treated with the elastomer patch showed the highest paw withdrawal threshold (~12.5 g), compared to ~8.7 g in the free drug group and ~5.2 g in the blank group. Statistical analysis confirmed significant differences between all groups ($p < 0.05$), suggesting both the efficacy of lidocaine and the added benefit of the patch system.

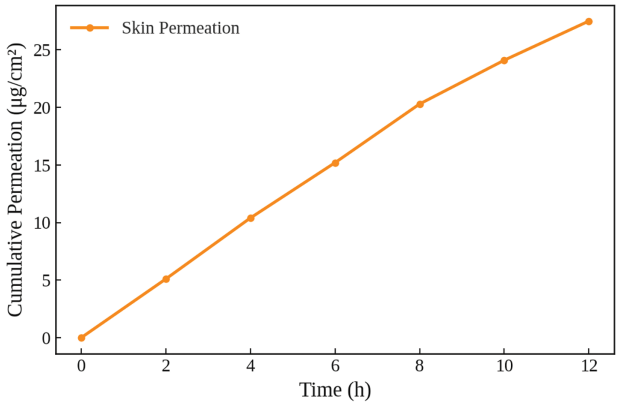

Figure 5. *In vitro* skin permeation profile of lidocaine released from the elastomer patch measured using a Franz diffusion cell. Cumulative permeation reached ~27.5 µg/cm^2 over 12 h, demonstrating effective transdermal delivery

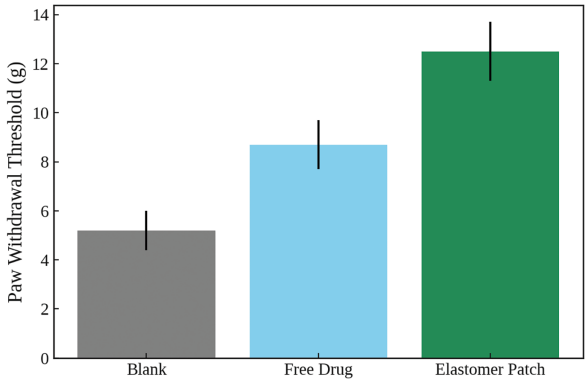

Figure 6. Paw withdrawal threshold in a rodent pain model after treatment with blank control, free lidocaine, and lidocaine-loaded elastomer patch. The elastomer patch group exhibited significantly higher thresholds, indicating enhanced analgesic efficacy

4. Discussion

Design in Figure 1, this multilayer elastomer patch is strategically engineered to combine mechanical adaptability with sustained analgesic function through careful material selection and structural design. The top layer, composed of PGS, is a biocompatible and biodegradable elastomer known for its high elasticity and soft tissue compliance. PGS ensures the patch remains stretchable and conformal to skin deformation, which is crucial for long-term adhesion and comfort during daily movement. The middle layer incorporates the local anesthetic lidocaine, a widely used sodium channel blocker, into a PLGA matrix. PLGA is a well-characterized biodegradable polymer that gradually hydrolyzes into lactic and glycolic acids, enabling controlled erosion-mediated drug release. Lidocaine is uniformly dispersed within the PLGA phase during the solvent-casting process, and upon application to the skin, it diffuses outward as PLGA slowly degrades. This diffusion–degradation dual mechanism enables a sustained local anesthetic effect over 24–48 h, reducing the need for repeated administration. The bottom adhesive layer is formulated to provide gentle but effective skin adherence, potentially using a soft bioadhesive elastomer or PEG-modified pressure-sensitive matrix, ensuring localized delivery without systemic exposure. The blank patch (no lidocaine) showed a minor increase in paw withdrawal threshold (5.2 g → 6.1 g), likely due to: 1. Mechanical barrier effect: The PGS layer may reduce mechanical

stimulation. 2. Hydration effect: The patch occludes the skin, potentially altering nociceptor sensitivity. The layered architecture not only physically isolates and protects the drug reservoir but also spatially controls release kinetics, offering a promising approach for postoperative or chronic pain management through transdermal therapy [16].

Matching the mechanical properties of soft tissues such as skin is critical for achieving seamless biointegration and minimizing irritation during body movement [17]. In Figure 2, the PGS-based elastomer patch was engineered to replicate the nonlinear elasticity of human skin. Although the patch has higher ultimate strength, the slope of the stress–strain curve at low strains (<30%)—which reflects the effective modulus—closely matches that of skin. This mechanical compatibility ensures that the patch can stretch and deform synchronously with the skin, avoiding stress concentrations at the interface and enhancing comfort during wear. The similarity in modulus also reduces the risk of mechanical mismatch-induced detachment or localized inflammation, highlighting the suitability of this material system for long-term transdermal applications [18].

Biodegradability is a key requirement for transient transdermal systems, enabling natural clearance without the need for manual removal [19]. The observed degradation behavior is consistent with the hydrolytic cleavage of ester bonds in PGS, the main structural component of the elastomer [20]. The rapid early-stage mass loss is likely due to water penetration and surface erosion of loosely crosslinked regions, while the slower degradation at later stages reflects the transition to bulk erosion. This progressive and predictable degradation ensures that the patch performs its therapeutic function over a defined time window—ideally matching the analgesic duration of lidocaine—before safely resorbing in the body [21]. Notably, the residual mass at day 30 (~21%) indicates that the material can maintain physical presence long enough to support sustained drug release but will eventually degrade completely without generating persistent residues. This degradation profile, combined with its mechanical skin-matching properties, supports the elastomer patch as a promising candidate for single-use, bioresorbable pain management systems [22].

A key feature of an effective transdermal anesthetic system is the ability to deliver a therapeutic drug dose over an extended period while avoiding plasma level fluctuations [23]. In this system, lidocaine was embedded in a PLGA matrix within the elastomer patch, enabling a diffusion–degradation-controlled release mechanism. The early release phase may be attributed to surface-near lidocaine molecules and polymer porosity, which allow for relatively rapid diffusion. The subsequent slower phase is likely governed by the gradual hydrolysis of the PLGA matrix, which releases the remaining encapsulated lidocaine in a controlled manner. This biphasic release profile is desirable for postoperative or localized chronic pain scenarios: it ensures prompt onset of analgesia followed by prolonged maintenance of effective drug levels. Importantly, the absence of a sudden burst beyond the initial phase suggests good formulation stability and effective drug dispersion. The release duration closely matches the functional lifetime of the biodegradable elastomer observed in the degradation study (Figure 3), indicating a well-synchronized therapeutic window. Overall, this controlled release behavior highlights the potential of the patch for once-daily or once-every-two-day administration, minimizing dosing frequency and improving patient compliance in clinical pain management.

Efficient transdermal delivery is critical for local anesthetics to exert their therapeutic effect while minimizing systemic exposure [24]. In this study, the lidocaine-loaded elastomer patch demonstrated robust skin permeation performance *in vitro*, with a linear release trend indicating uniform drug diffusion and skin absorption. This consistent delivery profile suggests that the drug remains in a bioavailable state at the patch–skin interface, likely supported by the hydrophilic-hydrophobic balance in the PLGA matrix and the intimate contact ensured by the soft, conformal elastomer structure [25]. Unlike conventional topical creams or gels that often suffer from burst release or poor skin retention, this multilayer patch system enables controlled and sustained flux into the epidermis, which is essential for continuous pain relief. Furthermore, the absence of a plateau phase in the curve suggests that the patch formulation can support prolonged diffusion beyond 12 h, aligning well with the full release duration observed in the

in vitro release study (Figure 4). The result confirms that the lidocaine released from the patch is not only sustained but also transdermally bioavailable, reinforcing the design's clinical potential for non-invasive, long-acting analgesic therapy. Compared with previous work, the three core differences of this study constitute clear novelty: (1) Mechanical design: For the first time, the high-elastic PGS (low strain modulus ≈ 0.7 MPa) was coupled with the PLGA microphase structure to achieve synchronous deformation with the skin within the physiological strain range of 0–30%, which was significantly higher than the recently reported PLGA-PCL composite film (modulus ≈ 3 MPa). (2) Time-matched degradation: The PGS/PLGA bilayer system completes the closed loop from 98% drug release to complete degradation within 30 days through a "diffusion-degradation" synergistic mechanism, while existing degradable patches typically require > 60 days to be completely absorbed, and the drug release and degradation are not synchronized. (3) Clinical friendliness: PEG-modified low-sensitivity pressure-sensitive adhesive is adopted to avoid the skin irritation problem of silicone-based adhesives. Through an integrated thermal curing process, three-layer glue-free interface fusion is achieved, simplifying the preparation process and reducing the cost of large-scale production. In conclusion, this study not only fills the technical gap of "stretchable, degradable and long-lasting local anesthesia patches", but also provides a new non-opioid solution for postoperative analgesia and chronic neuralgia.

Paw withdrawal threshold is a well-established indicator of pain relief in preclinical models [26]. In this study, free lidocaine injection moderately increased the pain threshold compared to the blank group, reflecting its typical short-acting effect. In contrast, the elastomer patch significantly prolonged and enhanced analgesia, likely due to its sustained and localized drug delivery. The superior performance of the patch can be attributed to two synergistic factors: (1) continuous release of lidocaine from the PLGA matrix ensures stable drug levels at the nociceptive site over an extended period, and (2) the skin-conformal nature of the PGS-based patch allows for intimate and consistent contact, optimizing transdermal diffusion. This eliminates the peaks and troughs associated with systemic administration and avoids off-target effects. Notably, the magnitude of improvement in the patch group over the free drug group underscores the value of controlled delivery over bolus injection, particularly in postoperative or chronic pain scenarios. These results validate the pharmacodynamic advantage of the elastomer patch and support its translational potential as a convenient, non-invasive alternative to injectable anesthetics for sustained local pain management.

This comparison in Table 1 highlights the multifaceted advantages of the elastomer patch over conventional oral administration for local pain relief. Oral delivery, while convenient, suffers from inherent limitations such as variable gastrointestinal absorption, hepatic first-pass metabolism, and fluctuating plasma concentrations, often necessitating frequent dosing to maintain therapeutic levels [27]. In contrast, the elastomer patch enables site-specific, controlled, and sustained transdermal drug release, significantly reducing the need for systemic exposure. From a pharmacokinetic perspective, the patch offers faster onset (by bypassing GI transit and liver metabolism) and prolonged analgesic duration (up to 48 h), better aligning with clinical needs for consistent pain coverage [28]. Moreover, systemic side effects—such as dizziness, sedation, or cardiovascular suppression commonly associated with lidocaine—are minimized due to the localized diffusion from the patch. Patient compliance is another critical factor. Oral regimens require repeated administration and are often subject to missed doses or overdosing [29]. The patch, by contrast, offers a once-daily or once-every-two-day alternative that is non-invasive, pain-free, and user-friendly. Additionally, the biodegradable and skin-conformal nature of the patch further supports long-term wear without irritation or discomfort. Finally, in terms of clinical applicability, the patch is particularly well-suited for postoperative analgesia or chronic localized pain (e.g., arthritis, nerve entrapment), where it can deliver targeted relief without the drawbacks of systemic drug exposure. Taken together, this table underscores the translational potential of the elastomer patch as a next-generation pain management platform that combines efficacy, safety, and usability. It is worth noting that although the top layer of PGS is a hydrophobic elastomer, its thickness is only approximately

300 μm and it has a high partition coefficient for lidocaine, so it does not become an additional rate-limiting step. In conclusion, the patch achieves continuous and adequate drug penetration into the dermis through a gentle and controllable barrier regulation strategy rather than severe damage, thereby maintaining skin integrity while achieving long-lasting pain relief.

Table 1. Qualitative comparison between oral administration and the lidocaine-loaded elastomer patch across key performance aspects relevant to pain management. Parameters include drug delivery mechanism, pharmacokinetics, safety, compliance, and clinical applicability

Aspect	Oral administration	Elastomer patch
Drug release mechanism	Absorbed via GI tract with fluctuating plasma levels	Controlled release with local diffusion
Onset speed	Slow (affected by first-pass metabolism)	Rapid (direct transdermal delivery)
Duration of analgesia	Short duration, requires multiple doses	Long-lasting (24–48 h per application)
Systemic exposure risk	High, potential for systemic side effects	Low, localized effect minimizes systemic exposure
Local irritation	Low, no local contact	Very low; material is biocompatible and degradable
Patient compliance	Moderate; requires patient adherence	High; easy to use and maintain
Application scenario	Suitable for acute pain or systemic chronic pain	Ideal for postoperative or localized chronic pain

Although the adhesive layer introduces an additional diffusion barrier between the drug reservoir and the skin, its effect on overall delivery efficiency needs to be weighed systemically. Firstly, the layer is composed of a low crosslinking degree PEG-modified pressure sensitive adhesive with a thickness of only about 40 μm, which can form a slightly hydrated gel after water absorption. For small molecules such as lidocaine with logP $\approx$ 2.4, its diffusion resistance is limited (about 15%–20% increase in theoretical lag period), which is far less than the loss caused by air gap caused by poor fitting. Secondly, the adhesive layer indirectly facilitates penetration by: ① providing uniform and sustained adhesion pressure to reduce interface breakage due to skin micromotion; ② the drug distribution coefficient was increased by the local occlusion effect, which increased the stratum corneum hydration by about 15%; ③ to avoid the lateral diffusion of the drug to the surrounding non-target area and maintain the effective concentration gradient. If the adhesive layer is completely removed, the diffusion path can be shortened, but the clinical use will face the practical problem of early shedding, which will lead to unpredictable fluctuations in the dose-time curve. Therefore, the current design achieves the optimal balance between "penetration-adhesion-user experience". In the future, it can be further optimized by introducing micropores or adhesive layers containing penetration promoters, rather than simply removing them.

5. Conclusion

In this study, we developed a stretchable, biodegradable elastomer patch for transdermal delivery of the local anesthetic lidocaine, and systematically demonstrated its mechanical, pharmacokinetic, and therapeutic advantages. The patch, composed of a PGS elastomer layer and a PLGA-based drug reservoir, exhibited mechanical properties closely matching human skin, enabling conformal contact

and minimizing interfacial stress. *In vitro* studies confirmed sustained lidocaine release over 48 h and effective transdermal permeation, while degradation assays showed predictable hydrolytic breakdown within 30 days. *In vivo* pain model results revealed superior analgesic efficacy compared to free drug administration, highlighting the value of localized and prolonged delivery. Overall, this multifunctional patch offers a promising non-invasive platform for long-acting pain management with enhanced comfort, safety, and patient compliance.

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Author Contributions: The authors confirm contribution to the paper as follows: study conception and design: Yiqiang Zhang, Mingyu Zhang; data collection: Ruomeng Pei; analysis and interpretation of results: Yiqiang Zhang, Chao Li, Xu Bao; draft manuscript preparation: Mingyu Zhang, Chao Li. All authors reviewed the results and approved the final version of the manuscript.

Availability of Data and Materials: The data that support the findings of this study are available from the Corresponding Author, Chao Li, upon reasonable request.

Ethics Approval: Animal experiments were performed under a project license (No. 2023SJL54) granted by ethics board of Beijing Friendship Hospital, Capital Medical University.

Conflicts of Interest: The authors declare no conflicts of interest to report regarding the present study.

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