List of Publications

Articles published in peer reviewed national/international journals:

(Cumulative impact factor: 130+; Citations: 300+; h-index: 8; i-10 index: 8)

1. **Souradeep Dey,** Amritha K Bhat, Janani G, Vartik Shandilya, Raghvendra Gupta and Biman B. Mandal. Microfluidic Human Physiomimetic Liver Model as a Screening Platform for Drug Induced Liver Injury. ***Biomaterials*** **(2024); (I.F. 12.8)**
2. Bibrita Bhar, Rajan Singh, Vaishak Ramesh, **Souradeep Dey**, Samit Nandi, Roy Paily and Biman B. Mandal. Wearable e-Bandage with Antimicrobial Ionogel as an Integrated Electroceutical Device for Accelerated Wound Healing. ***ACS Materials Letters*** **(2024); (I.F. 9.6)**
3. Ritvika Kushwaha, **Souradeep Dey**, Kanika Gupta, Biman B. Mandal and Debapratim Das. Secondary Chemical Cross-Linking to Improve Mechanical Properties in a Multifaceted Biocompatible Strain Sensor**.** ***ACS Applied Materials & Interfaces*** **(2024); (I.F. 8.3)**
4. Bibhas K. Bhunia, Ashutosh Bandyopadhyay, **Souradeep Dey** and Biman B. Mandal. Silk-hydrogel functionalized with human decellularized Wharton's jelly extracellular matrix (dWJECM) as a minimally invasive injectable hydrogel system for potential nucleus pulposus tissue replacement therapy. ***International Journal of Biological Macromolecules***. **(2024)**; **(I.F. 7.7)**
5. Rupam Khatua, Bibrita Bhar, **Souradeep Dey**, Chitra Jaiswal, Victoria J and Biman B. Mandal. Advances in Engineered Nanosystems: Immunomodulatory Interactions for Therapeutic Applications. ***Nanoscale*** **(2024)**; **(I.F. 5.8)**
6. Yogendra Pratap Singh, Ashutosh Bandyopadhyay, **Souradeep Dey**, Nandana Bhardwaj, Biman B. Mandal. Trends and Advances in Silk-Based Bioinks for Cartilage Tissue Engineering. ***Progress in Biomedical Engineering*****. (2024); (I.F. 5.0)**
7. Nandana Bhardwaj, **Souradeep Dey**, Bibrita Bhar and Biman B. Mandal. Bioprinted in vitro tissue models: An emerging platform for developing therapeutic interventions and disease modeling. ***Progress in Biomedical Engineering*****. (2023); (I.F. 5.0)**
8. Shreya Mehrotra, **Souradeep Dey**, Kunj Sachdeva, Sujata Mohanty and Biman B. Mandal. Recent advances in tailoring stimuli responsive hybrid scaffolds for cardiac tissue engineering and allied applications. ***Journal of Materials Chemistry B.*** **(2023); (I.F. 6.1)**
9. Swatilekha Hazra, **Souradeep Dey**, Biman B. Mandal and Charanya Ramachandran**.** In vitro profiling of extracellular matrix and integrins expressed by human corneal endothelial

cells cultured on silk fibroin-based matrices. ***ACS Biomaterials Science & Engineering.*** **(2023); (I.F. 5.4)**

10. Angana Borbora, Yang Xu, **Souradeep Dey**, Xin Wang, Yuxing Yao, Biman B. Mandal, Xiaoguang Wang and Uttam Manna. Lubricated Interfaces Enabling Simultaneous Pulsatile and Continuous Chemical Release Modes. ***Advanced Materials.*** **(2023); (I.F. 27.4)**
11. Joseph Christakiran Moses, **Souradeep Dey**, Ashutosh Bandyopadhyay, Manoj Agarwala, and Biman B. Mandal. Silk Based Bioengineered Diaphyseal Cortical Bone Unit Enclosing an Implantable Bone Marrow Towards Atrophic Non-union Grafting. ***Advanced Healthcare Materials***. (**2022)**; **(I.F. 10.0)**
12. G Janani, Smriti Priya, **Souradeep Dey** and Biman B. Mandal. Mimicking native liver lobule microarchitecture in vitro with parenchymal and non-parenchymal cells using 3D bioprinting for drug toxicity and drug screening applications. ***ACS Applied Materials & Interfaces*** **(2022)**; **(I.F. 8.3).**
13. Satyajit Mahata, **Souradeep Dey**, Biman B. Mandal, Vadivelu Manivannan. 3-(2-Hydroxyphenyl) imidazo [5, 1-α] isoquinoline as Cu (II) sensor, its Cu (II) ensemble for selective detection of CN^- ion and biological compatibility. ***Journal of Photochemistry and Photobiology A: Chemistry*****. (2022) (I.F. 4.1).**
14. Satyajit Mahata, Sandeep Kumar, **Souradeep Dey**, Biman B. Mandal, Vadivelu Manivannan. A probe with hydrazinecarbothioamide and 1,8-naphthalimide groups for "turn-on" fluorescence detection of Hg2+ and Ag+ ions. ***Inorganica Chimica Acta*****. (2022) (I.F. 2.7).**
15. **Souradeep Dey,** Chitra Jaiswal, Sayanti Shome, Bibrita Bhar, Ashutosh Bandyopadhyay, Kodieswaran Manikumar, Rajat Dadheech and Biman B. Mandal. Photocrosslinkable silk-based biomaterials for regenerative medicine and healthcare applications. ***Regenerative Engineering and Translational Medicine*****. (2022) (I.F. 2.2).**
16. Bibhas K. Bhunia*, **Souradeep Dey***, Ashutosh Bandyopadhyay and Biman B. Mandal. Design and fabrication of 3D-printed biomimetic construct to recapitulate form and function of intervertebral disc. ***Applied Materials Today*****; (2021)**; **(*equally contributed) (I.F. 7.2).**
17. Shreya Mehrotra, Rishabh Deo Singh, Ashutosh Bandyopadhyay, G. Janani, **Souradeep Dey** and Biman B. Mandal. "Engineering Microsphere-Loaded Non-mulberry Silk-Based 3D Bioprinted Vascularized Cardiac Patches with Oxygen-Releasing and Immunomodulatory Potential." ***ACS Applied Materials & Interfaces*** **(2021)**; **(I.F. 8.3).**

18. Ashutosh Bandyopadhyay, Suvro Kanti Chowdhury, **Souradeep Dey,** Joseph Christakiran Moses and Biman B. Mandal. Silk - A promising biomaterial opening new vistas towards affordable healthcare solutions. ***Journal of the Indian Institute of Science,*** 1-43. (**2019**); **(equally contributed) (I.F. 1.8)**

Book chapter(s)

1. Chitra Jaiswal, **Souradeep Dey**, Sayanti Shome, Gargi Mandal, Amritha K Bhat, Rupam Khatua, Animesh Mishra, Baishali Ghibhela, Eshani Das, Shruti More, Biman B. Mandal. Non-mulberry silk-based biomaterials: Biomedical applications, current status and future perspective. ***Silk-based Biomaterials for Tissue Engineering, Regenerative and Precision Medicine, Second Edition*. 2024**;

Patent(s) applied

1. Biman B. Mandal and **Souradeep Dey**. Microfluidic human physiomimetic liver model as a drug screening platform. **Date: 20.05.2024**

Conference proceeding(s)

1. **Souradeep Dey**, Pragya Mehra, Chitra Jaiswal, Bibrita Bhar and Biman B. Mandal. 3D Bioprinted Microphysiological In Vitro Osteochondral Model to Study Osteoarthritic Niche. Tissue Engineering Part A. 2024; S-193. **(I.F. 3.5)**
2. **Souradeep Dey,** Amritha K Bhat, Janani G, Ashutosh Bandyopadhyay, Vartik Shandilya, Raghvendra Gupta and Biman B. Mandal. Perfusion bioreactor-based 3D printed *in vitro* liver model for drug screening applications. ***Tissue Engineering Part A*. 2023;** 29 (13-14), PP-129. **(I.F. 3.5)**
3. **Souradeep Dey,** Triya Saha and Uttamchand Narendrakumar. Analysis of Urine as Indicators of Specific Body Conditions. ***IOP Conf. Ser.: Mer. Sci. Eng.* 2017**; 263 022051.

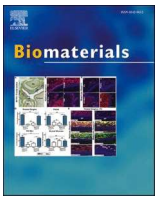
Due to file size limitations only the first two pages of the 02 publications are attached below.

Biomaterials 310 (2024) 122627

Contents lists available at ScienceDirect

Biomaterials

journal homepage: www.elsevier.com/locate/biomaterials



Microfluidic human physiomimetic liver model as a screening platform for drug induced liver injury

Souradeep Dey [a], Amritha Bhat [b], G. Janani [b], Vartik Shandilya [c], Raghvendra Gupta [a,c,d], Biman B. Mandal [a,b,d,*]

[a] Centre for Nanotechnology, Indian Institute of Technology Guwahati, Guwahati, 781039, Assam, India
[b] Biomaterials and Tissue Engineering Laboratory, Department of Biosciences and Bioengineering, Indian Institute of Technology Guwahati, Guwahati, 781039, Assam, India
[c] Department of Chemical Engineering, Indian Institute of Technology Guwahati, Guwahati, 781039, Assam, India
[d] Jyoti and Bhupat Mehta School of Health Sciences and Technology, Indian Institute of Technology Guwahati, Guwahati, 781039, Assam, India

ARTICLE INFO

Keywords:
Human liver model
Drug screening
Drug induced liver injury
Hepatotoxicity
3D printing
Cell instructive biomaterial ink
Physiomimetic microfluidic device

ABSTRACT

The pre-clinical animal models often fail to predict intrinsic and idiosyncratic drug induced liver injury (DILI), thus contributing to drug failures in clinical trials, black box warnings and withdrawal of marketed drugs. This suggests a critical need for human-relevant in vitro models to predict diverse DILI phenotypes. In this study, a porcine liver extracellular matrix (ECM) based biomaterial ink with high printing fidelity, biocompatibility and tunable rheological and mechanical properties is formulated for supporting both parenchymal and non-parenchymal cells. Further, we applied 3D printing and microfluidic technology to bioengineer a human physiomimetic liver acinus model (HPLAM), recapitulating the radial hepatic cord-like structure with functional sinusoidal microvasculature network, biochemical and biophysical properties of native liver acinus. Intriguingly, the human derived hepatic cells incorporated HPLAM cultured under physiologically relevant microenvironment, acts as metabolic biofactories manifesting enhanced hepatic functionality, secretome levels and biomarkers expression over several weeks. We also report that the matured HPLAM reproduces dose- and time-dependent hepatotoxic response of human clinical relevance to drugs typically recognized for inducing diverse DILI phenotypes as compared to conventional static culture. Overall, the developed HPLAM emulates in vivo like functions and may provide a useful platform for DILI risk assessment to better determine safety and human risk.

1. Introduction

DILI is a patient specific, temporal, multifaceted pathophysiological process in response to drugs or other xenobiotics that arises either as a predictable event or as an unpredictable event leading to loss of both parenchymal and non-parenchymal cells [1]. Typically, DILI is classified into intrinsic and idiosyncratic hepatotoxicity based on the mechanism of action of the chemical compound. The intrinsic type is direct, dose related, predictable and occurs at a short duration in individuals exposed to certain threshold level of drugs. In contrast, idiosyncratic type is drug dose independent, has a longer latency period, is triggered by the interaction of drug with the host and environmental factors and occurs mainly after re-exposure [2,3].

The U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) requires the evaluation of new drug candidates in animal models, before initiating human clinical trials of a new chemical entity [3–5]. However, an analysis of 150 drugs in animals that caused adverse reactions in humans, reported the concordance of hepatotoxicity finding between animals studies and observed human toxicities to be only 55 % [6]. The major reason for this low concordance is hypothesized to be the genetic variations, mechanism of toxicity and drug metabolizing pathways that involves the differences in drug metabolizing enzyme and transporter expressions [1,7]. Furthermore, DILI in humans is typically not identified until clinical trials or post-marketing, leading to an increased risk of hepatotoxicity in clinical trial participants as well as a financial burden in the drug development pipeline. Thus, a

* Corresponding author. Department of Biosciences and Bioengineering, Centre for Nanotechnology and Jyoti and Bhupat Mehta School of Health Sciences and Technology, Indian Institute of Technology Guwahati, Assam, India.
E-mail addresses: biman.mandal@iitg.ac.in, mandal.biman@gmail.com (B.B. Mandal).

https://doi.org/10.1016/j.biomaterials.2024.122627
Received 18 January 2024; Received in revised form 2 May 2024; Accepted 19 May 2024
Available online 21 May 2024

paradigm shift in reduction, replacement and refinement (3'Rs' principle) of animal models is desired from the pharmaceutical and biotechnology industries which serves the critical need for the development of more predictive and human-relevant in vitro models for improved hepatotoxicity testing.

Moreover, the FDA centre for drug evaluation and research, EMA and the Government of India's "New Drugs and Clinical Trials (Amendment) Rules, 2023" also encourages the adoption of in silico and in vitro models to improve the regulatory efficiency and expedite drug development [8–10]. In order to drive a paradigm shift in the use of non-animal methods for drug discovery and development pipelines, conventional 2D coculture, 3D spheroid and 3D dense constructs based

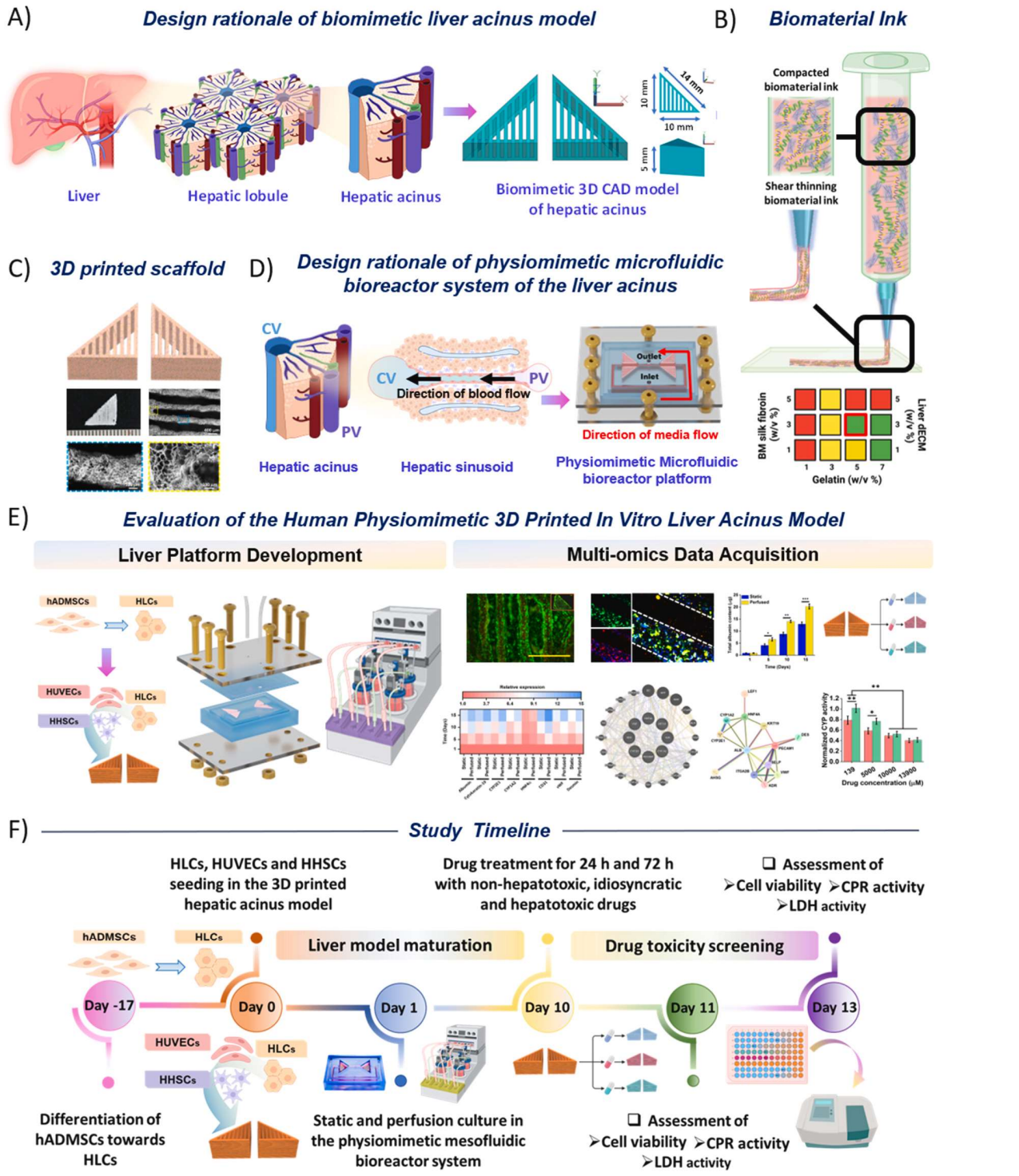


Fig. 1. Schematic representation of the rationale and timeline of the study; A) Illustration of the native hepatic acinus inspired development of the biomimetic CAD model of the 3D scaffold; **B)** Schematic representation of the biomaterial ink formulation and its characterization; **C)** Illustration of the 3D printed biomimetic liver acinus scaffold and its characterization; **D)** Scheme representing the native human liver acinus microphysiological environment inspired conceptualization of human physiomimetic liver microfluidic bioreactor platform **E)** Illustration of the overall development and functional evaluation of the human physiomimetic in vitro liver acinus model **F)** The timeline of the vital experimental steps followed in the study. Created with BioRender.com.

ADVANCED MATERIALS
www.advmat.de

Lubricated Interfaces Enabling Simultaneous Pulsatile and Continuous Chemical Release Modes

Angana Borbora, Yang Xu, Souradeep Dey, Xin Wang, Yuxing Yao, Biman B. Mandal, Xiaoguang Wang,* and Uttam Manna**

The release of chemicals following either pulsatile or continuous release modes is important for various potential applications, including programmed chemical reactions, mechanical actuation, and treatments of various diseases. However, the simultaneous application of both modes in a single material system has been challenging. Here, two chemical loading methods are reported in a liquid-crystal-infused porous surface (LCIPS) that enables both a pulsatile and continuous release of chemicals simultaneously. Specifically, chemicals loaded in the porous substrate exhibit a liquid crystal (LC) mesophase-dependent continuous release, whereas the chemicals dissolved in micrometer-sized aqueous droplets dispersed in the LC surface follow a pulsatile release activated by a phase transition. Moreover, the loading method of distinct molecules can be controlled to program their release mode. Finally, the pulsatile and continuous release of two distinct bioactive small molecules, tetracycline and dexamethasone, are demonstrated which display antibacterial and immunomodulatory activities for applications such as chronic wound healing and biomedical implant coating.

1. Introduction

The manipulation of the release mode of drugs and chemicals is critical for theranostics and material synthesis. Continuous release (i.e., the gradual release of loaded chemicals for a prolonged duration with a slow or modulated release rate)[1] and pulsatile release (i.e., the abrupt release of loaded chemicals within a short time)[2] are the two elemental release modes for the treatment of different types of diseases.[1,2,3] For example, a continuous release is vital for the treatment of glaucoma,[4] cancer,[5] asthma,[6] cardiovascular disease,[7] etc., where the drug efficacy needs to be maintained for an extended period without frequent use of a high dosage.[1a] In contrast, a pulsatile release is critical for the treatment of diseases such as inflammatory diseases,[8] acute gastritis,[9] diabetes,[10] rheumatoid arthritis,[11] and so on, requiring an adequate dose of a specific drug at definite time intervals to minimize the delay in treatment.[12] Practical biomedical applications often require a combination of the above two release modes to achieve effective combinatorial treatment. For example, the implantation of medical devices for therapeutic application[13] or wound healing requires continuous antibiotics to circumvent bacterial infections[14] and pulsatile doses of

A. Borbora, U. Manna
Bio-Inspired Polymeric Materials Lab
Department of Chemistry
Indian Institute of Technology Guwahati
Guwahati, Assam 781039, India
E-mail: umanna@iitg.ac.in

Y. Xu, X. Wang
William G. Lowrie Department of Chemical and Biomolecular Engineering
The Ohio State University
Columbus, OH 43210, USA
E-mail: wang.12206@osu.edu

S. Dey, B. B. Mandal, U. Manna
Centre for Nanotechnology
Indian Institute of Technology Guwahati
Guwahati, Assam 781039, India
E-mail: biman.mandal@iitg.ac.in

X. Wang
Smith School of Chemical and Biomolecular Engineering
Cornell University
Ithaca, NY 14850, USA

Y. Yao
Division of Chemistry and Chemical Engineering
California Institute of Technology
Pasadena, CA 91125, USA

B. B. Mandal
Biomaterials and Tissue Engineering Laboratory
Department of Biosciences and Bioengineering
Indian Institute of Technology Guwahati
Guwahati, Assam 781039, India

B. B. Mandal, U. Manna
Jyoti and Bhupat Mehta School of Health Sciences and Technology
Indian Institute of Technology Guwahati
Guwahati, Assam 781039, India

X. Wang
Sustainability Institute
The Ohio State University
Columbus, OH 43210, USA

The ORCID identification number(s) for the author(s) of this article can be found under https://doi.org/10.1002/adma.202302264

DOI: 10.1002/adma.202302264

bioactive/immunomodulatory molecules to facilitate stem cell differentiation[15] or immunomodulation.[16] State-of-the-art chemical release systems, such as the layer-by-layer assembly of polymers,[15,17] phospholipid cubosomes,[18] hydrogel,[5,12,14,19] and water microdroplets dispersed in liquid crystal (LC) surfaces,[20] can perform only one type of release at a time. The simultaneous release from a single material system of the same or different chemicals in both an on-demand pulsatile and a continuous mode has been a substantial challenge.

Combinatorial drug delivery following distinct release modes is often necessary for practical biomedical applications to effectively treat chronic diseases. For example, chronic diabetic wounds are a major complication for diabetic patients, increasing the risk of clinical infection and ultimately leading to limb amputation. Unlike acute wounds, diabetic wounds fail to heal due to perpetual hyperglycemia, which triggers a chronic inflammatory response, infection, and growth factor degradation at the wound site, interrupting the dynamic process of wound healing.[21] Therefore, effective treatment of diabetic wound healing requires a combinatorial drug delivery approach to modulate inflammation, prevent infection, and promote tissue regeneration.[19g,21c,22] Various drug-release strategies have been developed to accelerate diabetic wound healing by modulating the immune system and preventing bacterial infection.[19g,23] One effective strategy is a dual-mode drug-releasing system with a continuous and sustained antibacterial drug release and an instantaneous triggered immunomodulatory drug release to prevent a pro-inflammatory microenvironment in response to potential bacterial invasion.[23b-d,24] Similarly, a dual mode of drug release is also found to be effective in cancer treatment. For instance, the paclitaxel and curcumin loaded nanocarrier demonstrates continuous and sustained drug release due to enzyme hydrolysis and hydrophobic interactions, while a triggered rapid release of drug is observed when exposed to NIR laser. Evaluation of this versatile stimuli-responsive dual drug-release approach demonstrates an effective synergistic anticancer effect both in vitro and in vivo.[25]

Herein, we report the design of a liquid-crystal-infused porous surface (LCIPS) with two chemical loading methods that enable a simultaneous chemical release in both pulsatile and continuous modes. The two release modes are designed to function independently, allowing the same or different chemicals or drugs to be released in either mode. The inherent phase transition properties of the LC are used to modulate these two release modes. The versatility of the release system is further demonstrated using two distinct bioactive molecules, with the continuous release of antibiotics acting against bacteria growth and the pulsatile release of anti-inflammatory drugs attesting to on-demand immunomodulatory effects. Overall, the results reported in this work provide a design principle for the programmable release of chemicals and drugs, which have potential uses in the combinatorial treatment of multiple diseases[26] or as a biomedical implant coating with multifunctional traits.[27]

2. Results and Discussions

2.1. Preparation of Liquid-Crystal-Infused Porous Surface

To study the LC-mediated chemical release behaviors, we prepared a chemically reactive porous polymeric substrate to stabilize the LC against water-induced dewetting. As schemed in **Figure 1**a, we performed a 1,4-conjugate addition reaction between branched polyethylenimine and dipentaerythritolpentaacrylate to form a porous polymeric network on a glass substrate via layer-by-layer deposition of a chemically reactive nanocomplex and branched polyethylenimine.[28] The size of the nanocomplex was characterized by dynamic light scattering (DLS, Figure S1a, Supporting Information). In addition, the prominent existence of attenuated total reflectance-Fourier transform infrared spectroscopy (ATR-FTIR) signatures for the C–H of vinyl and carbonyl stretching at 1409 cm^{-1} and 1734 cm^{-1}, respectively, confirm the presence of residual acrylate groups in the porous surface (Figure S1b, Supporting Information). Next, the prepared chemically reactive porous polymeric substrate is hydrophobically functionalized with selected alkylamine to stabilize the infused LC against dewetting by water (Figure 1c; Figure S2, Supporting Information, see Methods for details). As shown in Figure 1d,e, the morphology of the porous nanocomplex aggregates was characterized by field-emission scanning electron microscopy (FESEM).

To prepare an LCIPS, we used 4'-octyl-4-biphenylcarbonitrile (8CB), as it exhibits distinct mesophases with different molecular mobility and orientation (Figure 1b). We infused 8CB (30 µL) into the prepared porous polymeric substrate to form a 100 µm-thick 8CB film. We measured the contact angle of a water droplet to be ~75.8° on LCIPS irrespective of the LC mesophase (Figure 1f–i). Prior to lubrication, the beaded water droplet was pinned on the porous polymeric substrate (Figure 1j) and slid at different tilting angles after LC infusion, as shown in Figure 1k–m. The LC mesophase-dependent sliding angle of the beaded water droplet is in qualitative agreement with past studies.[20d,29] It is worth noting that the hydrophobic modification (Figure S2, Supporting Information) of the porous coating allows for the stabilization and locking of the LC within the coating, preventing its flow into the surrounding environment.

2.2. Continuous Release from LCIPS

In this research, we sought to use different loading methods to tune the chemical release mode from an LCIPS. In the first set of experiments, we loaded rhodamine B into the pores of the polymeric substrate by soaking it with a rhodamine B ethanol solution, and the solvent was evaporated before infusing the porous polymer substrate with 8CB, as schemed in **Figure 2**a. The loading of rhodamine B in the porous substrate was confirmed with fluorescence micrographs that can be found in Figure S3 (Supporting Information). Next, the rhodamine–B-loaded substrate was infused with 8CB to create an LCIPS. To demonstrate the continuous release of rhodamine B from the substrate through the LC surface layer, a 20 µL water droplet was placed on the rhodamine–B-loaded LCIPS. The temperature was then set to 25 °C, 35 °C, and 45 °C to transition the infused LC surface into the smectic A, nematic, and isotropic phases, respectively. As shown in Figure 2b and Figure S4 (Supporting Information), we observed a gradual coloration of the water droplets, suggesting a continuous release of rhodamine B from the porous polymeric substrate through the infused LC surface.

We attribute this continuous release to the size of rhodamine B being smaller than $K/W \approx 1$ µm, where K ($\approx 10^{-11}$ N)[30] is the elas-

