Bioinspired and Biomimetic Approaches in Transdermal Drug Delivery Systems: Innovations, Mechanisms, and Future Perspectives

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Abstract:

Transdermal drug delivery systems (TDDS) have emerged as a promising alternative to oral and injectable routes, offering sustained release, improved patient compliance, and reduced systemic side effects. However, the skin's stratum corneum presents a formidable barrier to efficient permeation, limiting the delivery of large or hydrophilic molecules. To overcome these challenges, bioinspired and biomimetic strategies have been extensively explored, drawing on principles observed in nature to design advanced carriers and devices. This review highlights innovations such as microneedles inspired by porcupine quills and mosquito proboscises, lipid-based vesicular carriers mimicking cell membranes, and biopolymer-based systems employing chitosan, silk fibroin, and hyaluronic acid. Additionally, smart and responsive systems, including pH-sensitive, enzyme-triggered, and temperature-responsive patches, offer adaptive drug release aligned with physiological conditions. The integration of nanotechnology, hydrogels, and bioelectronics has further advanced TDDS for chronic disease management, wound healing, and hormone therapy. Despite significant progress, challenges remain in large-scale production, regulatory approval, and long-term safety. Future research promises integration with artificial intelligence and the Internet of Things, paving the way for personalized and adaptive therapies. Bioinspired TDDS hold the potential to revolutionize non-invasive drug delivery, reshaping modern pharmacotherapy.

Keywords: Transdermal drug delivery, Bioinspired systems, Biomimetic formulations, Microneedles, Smart patches

1. Introduction

Overview of Transdermal Drug Delivery Systems (TDDS)

Transdermal Drug Delivery Systems (TDDS) are innovative pharmaceutical technologies that facilitate the administration of drugs through the skin, bypassing the gastrointestinal tract and liver(1). TDDS provides a controlled, sustained release of therapeutic agents over extended periods, improving patient compliance, reducing side effects, and enhancing the bioavailability of drugs(2). These systems typically consist of a drug reservoir or matrix, a rate-controlling membrane, and an adhesive layer for skin application(3). TDDS continuous or prolonged therapeutic effects, such as hormone replacement therapies require, pain management, and nicotine cessation products(4).This delivery method has garnered significant interest due to its non-invasive nature and ability to achieve consistent plasma drug levels(5). The key challenge, however, is overcoming the skin's natural barrier properties, primarily the stratum corneum, which hinders the effective penetration of large molecules or hydrophilic drugs(6). Various technologies, such as iontophoresis, microneedles, and electroporation, have been explored to enhance drug permeability through the skin, making TDDS a promising platform for a wide range of therapeutic applications(7).

Importance of Bioinspired and Biomimetic Strategies in Drug Delivery

Bioinspired and biomimetic strategies in drug delivery aim to replicate the principles observed in nature, enhancing the effectiveness and precision of drug delivery systems(8). These approaches often focus on mimicking biological processes such as cellular interactions, skin permeability mechanisms, or natural drug transporters to achieve efficient transdermal delivery(9). By leveraging nature’s designs, these strategies seek to optimize drug absorption and target specific tissues with minimal invasiveness(10). For example, bioinspired structures like liposomes or nanoparticles can be employed to mimic cellular membranes, facilitating drug release while protecting the drug from degradation(11). Biomimetic designs can also enhance targeting, improve drug solubility, and reduce side effects(12). Moreover, these approaches could significantly reduce the need for harsh chemicals or invasive techniques, thus aligning with the increasing demand for more sustainable and patient-friendly drug delivery solutions(13). The incorporation of such principles into TDDS offers a potential pathway for improving the transdermal delivery of biologics and large molecular drugs, expanding the scope of this technology beyond small-molecule therapeutics(14).

Scope and Objectives of the Review

This review aims to explore the cutting-edge innovations in bioinspired and biomimetic approaches within the field of transdermal drug delivery systems(15). The scope includes a detailed discussion of various bioinspired materials, such as natural polymers, skin-mimicking hydrogels, and nanoparticles, that have been successfully utilized to enhance skin penetration and drug release kinetics(16). It will also examine novel technologies such as microneedle arrays, lipid-based carriers, and iontophoretic systems that are inspired by biological mechanisms(17). The objectives of this review are to provide an overview of the principles and mechanisms behind these advanced systems, highlight recent advancements, and explore the challenges and future perspectives in this domain(18). Furthermore, the review will discuss the potential of these strategies for delivering both small molecules and biologics transdermally, addressing the opportunities and obstacles in scaling these innovations for commercial use(19).

Through this review, we aim to foster a deeper understanding of how bioinspired and biomimetic techniques can reshape the future of transdermal drug delivery, leading to more efficient, targeted, and patient-friendly therapies(20).

2. Fundamentals of Transdermal Drug Delivery

Skin Structure and Barrier Function

The skin is a highly complex organ that serves as a protective barrier, preventing harmful substances from entering the body while regulating fluid loss(21). It consists of three main layers: the epidermis, dermis, and hypodermis. The outermost layer, the **epidermis**, plays a critical role in drug delivery(22). The **stratum corneum**, the outermost part of the epidermis, is composed of dead skin cells and acts as the primary barrier to drug penetration(23). Beneath the epidermis lies the **dermis**, which contains blood vessels, nerves, and connective tissue, while the **hypodermis** consists of fat and connective tissue, serving as an energy reserve(24). The skin's barrier function arises from the stratum corneum's tightly packed keratinocytes and lipid-rich extracellular matrix, which restrict drug movement(25). This structure is highly selective, allowing only small, lipophilic molecules to pass through efficiently(26). Overcoming this barrier is essential for the effective delivery of drugs via the transdermal route(27).

Mechanisms of Drug Permeation Through the Skin

Drug permeation through the skin typically occurs through passive diffusion, where drugs move from an area of high concentration (on the surface of the skin) to an area of low concentration (inside the body)(28). The rate of permeation depends on factors such as drug size, molecular weight, solubility, and the nature of the skin layers(29). Two main routes are involved: **intercellular diffusion**, where drugs pass between the skin cells, and **transcellular diffusion**, where drugs pass directly through the cells(30). The most effective permeation route is typically intercellular, where lipophilic drugs move through the lipid-rich extracellular space. For hydrophilic drugs, permeation is more difficult due to the low permeability of the stratum corneum to water-soluble substances(31). To improve permeation, various methods like chemical enhancers, physical methods (e.g., microneedles, iontophoresis), and formulations (e.g., liposomes) are used to alter skin properties or disrupt the stratum corneum's integrity(32).

Challenges in Transdermal Drug Delivery and the Need for Novel Approaches

While transdermal drug delivery offers many advantages, several challenges hinder its widespread application(33). The primary barrier to effective drug permeation is the **stratum corneum**, which limits the absorption of most drugs, particularly large, hydrophilic molecules and biologics(34). Additionally, achieving sustained and controlled drug release without causing skin irritation or toxicity remains a complex issue. Some drugs may also degrade when exposed to the skin, reducing their therapeutic efficacy(35). The variability in individual skin properties, such as thickness, hydration, and age, further complicates transdermal delivery(36).The methods to enhance drug penetration, such as chemical enhancers or physical devices (e.g., microneedles, electroporation), often have limitations in terms of efficiency, safety, or Current patient comfort(37). As a result, there is a growing need for **novel approaches** in transdermal drug delivery, including bioinspired and biomimetic systems that can mimic natural skin structures, improve drug solubility, enhance permeability, and allow for precise control over drug release(38). These innovations could overcome the inherent challenges, expand the range of drugs suitable for transdermal delivery, and improve patient compliance and therapeutic outcome(39).

3. Bioinspired Strategies for Enhancing Transdermal Drug Delivery

Micro/Nanostructures Inspired by Nature (e.g., Micropillars, Nanoneedles)

Micro and nanostructures inspired by nature, such as **micropillars** and **nanoneedles**, mimic natural systems to enhance skin penetration and drug delivery(40). These structures are designed to create micro-channels or pores in the stratum corneum, bypassing the skin's natural barrier(41). Micropillars, inspired by natural surfaces like plant cuticles or insect exoskeletons, can puncture the skin without damaging deeper tissues, allowing controlled drug release(42). Similarly, **nanoneedles** are inspired by the microscopic structures found in certain plants and animals, providing a minimally invasive way to transport drugs across the skin(43). These bioinspired micro/nanostructures not only enhance skin permeability but also promote targeted, sustained drug delivery with reduced discomfort and irritation, offering an alternative to traditional methods like patches or injections(44).

Table 1: Bioinspired Strategies for Enhancing Transdermal Drug Delivery

Strategy	Description	Example
Micro/Nanostructures	Mimic natural structures to enhance skin penetration.	Micropillars, Nanoneedles
Biological Transport Mechanisms	Use vesicles similar to cell membranes for drug transport.	Liposomes, Niosomes
Biopolymer-Based Carriers	Natural polymers enhance drug absorption and biocompatibility.	Chitosan, Silk Fibroin, Hyaluronic Acid

Biological Transport Mechanisms (e.g., Lipid-Based Vesicular Systems Mimicking Cell Membranes)

Lipid-based vesicular systems, such as **liposomes** and **niosomes**, mimic the structure of natural cellular membranes to improve transdermal drug delivery(45). These vesicles are composed of lipid bilayers that resemble cell membranes, allowing them to merge with the skin’s lipid-rich layers for enhanced drug release(46). By encapsulating drugs within these vesicles, the drugs are protected from enzymatic degradation and controlled for sustained release(47). This bioinspired approach also increases the solubility of hydrophobic drugs and facilitates targeted drug delivery to specific skin layers or tissues(48). Additionally, these systems can improve skin penetration by interacting with the lipid matrix of the stratum corneum, offering a non-invasive, effective way to deliver both small molecules and larger biologics across the skin(49).

Biopolymer-Based Drug Carriers (e.g., Chitosan, Silk Fibroin, and Hyaluronic Acid)

Biopolymer-based drug carriers, such as **chitosan**, **silk fibroin**, and **hyaluronic acid**, leverage natural polymers to enhance drug delivery through the skin(50). **Chitosan**, a biopolymer derived from chitin, has antimicrobial properties and promotes skin penetration due to its ability to form biodegradable films(51). **Silk fibroin**, derived from silk, is a versatile biopolymer with excellent biocompatibility and controlled drug release properties, ideal for enhancing transdermal drug delivery(52). **Hyaluronic acid**, a naturally occurring polysaccharide in the skin, is known for its hydration properties, which can improve the permeation of drugs by increasing skin moisture content(53). These biopolymers are biodegradable, biocompatible, and provide a sustainable method for controlled and targeted drug release, making them ideal candidates for enhancing the performance of transdermal drug delivery systems(54).

4. Biomimetic Formulations for Improved Skin Penetration

Lipid-Based Biomimetic Carriers (Liposomes, Ethosomes, Niosomes)

Lipid-based **biomimetic carriers**, such as **liposomes**, **ethosomes**, and **niosomes**, are designed to mimic the structure of natural cell membranes, enhancing drug penetration through the skin(55). **Liposomes** are spherical vesicles composed of phospholipid bilayers that can encapsulate both hydrophilic and lipophilic drugs, protecting them from degradation and promoting sustained release(56). **Ethosomes** are similar but contain ethanol, which helps increase the fluidity of the lipid membrane, improving drug penetration through the skin's stratum corneum(57). **Niosomes**, made from non-ionic surfactants, offer similar benefits to liposomes but with greater stability and lower production costs(58). These lipid-based carriers enhance skin penetration by fusing with the lipid layers of the skin, facilitating drug release and improving the efficacy of transdermal delivery systems(59).

Table 2: Biomimetic Formulations for Improved Skin Penetration

Formulation Type	Mechanism	Example
Lipid-Based Carriers	Mimic cell membranes to improve drug solubility and stability.	Liposomes, Ethosomes, Niosomes
Peptide & Protein-Inspired Enhancers	Facilitate drug permeation via natural transport pathways.	Cell-Penetrating Peptides (CPPs)
Hydrogel Patches	Provide sustained drug release while maintaining skin hydration.	Biomimetic Hydrogels

Peptide and Protein-Inspired Penetration Enhancers

Peptide and protein-inspired penetration enhancers are biomimetic agents designed to improve the transdermal permeability of drugs by mimicking the natural transport mechanisms in the skin(60). **Cell-penetrating peptides (CPPs)**, derived from proteins, can transiently disrupt the stratum corneum or interact with cellular membranes, creating temporary channels that facilitate the movement of drugs across the skin barrier(61). These peptides can enhance the penetration of large molecules, such as proteins or nucleic acids, which typically face difficulties crossing the skin(62). By utilizing the mechanisms that allow peptides and proteins to naturally enter cells or tissues, these enhancers offer a targeted, non-invasive strategy to improve drug delivery efficiency(63).

Biomimetic Hydrogel Patches for Sustained Drug Release

Biomimetic hydrogel patches are advanced transdermal drug delivery systems that mimic the properties of natural tissues, providing controlled, sustained drug release(64). These hydrogels are typically composed of natural or synthetic polymers and incorporate water-absorbing structures similar to those found in human tissues(65). By adjusting the polymer network, these patches can provide a controlled release of the drug over a prolonged period, mimicking the natural diffusion processes in biological systems(66). The hydrogels' ability to maintain skin hydration while delivering drugs makes them particularly useful for delivering hydrophilic or large-molecular-weight drugs(67). These formulations offer superior skin compatibility, biocompatibility, and moisture retention, ensuring continuous drug release without the need for frequent reapplication, improving patient compliance and therapeutic outcomes(68).

5. Microneedle Technology: Learning from Nature

Porcupine Quill-Inspired Microneedles for Painless Drug Delivery

Porcupine quill-inspired microneedles leverage the natural structure of porcupine quills, which are sharp, stiff, and effective at penetrating the skin without causing significant pain. These microneedles are designed with similar sharpness and tapered tips, allowing them to pierce the stratum corneum with minimal discomfort(69). Their design ensures a quick and efficient drug delivery, reducing the invasiveness of traditional needles. This bioinspired approach helps make microneedle-based transdermal systems more patient-friendly, particularly for individuals who fear injections or need frequent medication administration(70).

Table 3: Microneedle Technology Inspired by Nature

Microneedle Type	Bioinspiration	Key Benefit
Porcupine Quill-Inspired	Mimics sharp, barbed structure of porcupine quills	Painless drug delivery with efficient skin penetration
Mosquito Proboscis-Inspired	Based on flexible and thin mosquito mouthparts	Minimal skin damage and reduced irritation
Dissolvable Microneedles	Made from biocompatible dissolvable materials	Controlled drug release without need for removal

Mosquito Proboscis-Inspired Microneedles for Minimal Skin Damage

Mosquito proboscis-inspired microneedles are modeled after the fine, delicate structure of mosquito proboscises, which can penetrate the skin with minimal damage while extracting blood. These microneedles are designed to mimic the thin, flexible nature of the mosquito proboscis, enabling painless and precise drug delivery(71). By mimicking the natural fluid extraction capabilities, they cause minimal tissue disruption, reducing the risk of irritation or inflammation(72). This bioinspired microneedle design enhances the efficiency of transdermal drug delivery while improving patient comfort and reducing adverse effects associated with needle use(73).

Bioinspired Dissolvable Microneedles for Controlled Drug Release

Bioinspired dissolvable microneedles are designed to deliver drugs efficiently while dissolving in the skin, eliminating the need for needle removal. These microneedles are often made from biocompatible materials like **hyaluronic acid** or **chitosan**, inspired by natural polymers that break down in the body(74). Upon skin insertion, the microneedles dissolve, releasing the drug in a controlled manner over time. This bioinspired approach not only enhances patient comfort but also ensures sustained drug delivery without the risk of needle reuse or disposal, making it ideal for vaccines and other therapeutic treatments(75).

6. Smart and Responsive Bioinspired TDDS

pH-Responsive Biomimetic Patches

pH-responsive biomimetic patches are designed to release drugs in response to the skin's pH changes, mimicking natural physiological processes(76). These patches use pH-sensitive polymers or hydrogels that swell or shrink depending on the local pH, enabling controlled drug release(77). For example, they may release drugs more effectively in areas with altered pH, such as inflamed or diseased skin. This bioinspired approach ensures targeted delivery, improving the therapeutic efficacy and reducing side effects by releasing drugs only when needed(78).

Table 4: Smart and Responsive Bioinspired TDDS

Type of Smart TDDS	Stimulus	Mechanism of Action
pH-Responsive Patches	Skin pH changes	Releases drugs in response to pH variations in inflamed or diseased skin
Enzyme-Triggered Systems	Specific skin enzymes	Drug is released when enzymes degrade the carrier material
Temperature & Moisture-Responsive TDDS	Environmental conditions	Hydrogels swell/shrink to regulate drug release

Enzyme-Triggered Drug Release Inspired by Biological Systems

Enzyme-triggered drug release is inspired by biological systems where enzymes regulate the release of substances at specific sites(79). These TDDS use biodegradable polymers or carriers that are sensitive to specific enzymes present in the skin or bloodstream. Upon encountering the enzyme, the carrier breaks down, releasing the encapsulated drug(80). This bioinspired approach ensures targeted drug delivery, mimicking the natural release processes of biological systems, and minimizes systemic side effects by releasing drugs only at the intended site of action(81).

Temperature and Moisture-Responsive TDDS

Temperature and moisture-responsive TDDS are designed to adjust drug release based on environmental stimuli like temperature or humidity(82). Inspired by natural processes that adapt to environmental changes, these systems use materials that change their physical properties in response to temperature or moisture fluctuations(83). For example, hydrogels or polymers may swell or shrink with temperature or moisture changes, controlling drug release rates. This responsiveness ensures that drugs are delivered more efficiently under specific conditions, offering more precise control over therapy and enhancing patient compliance by aligning with the body's natural variability(84).

7. Applications of Bioinspired TDDS in Disease Management

Transdermal Patches for Pain Management (Opioids, NSAIDs, Anesthetics)

Bioinspired transdermal patches for pain management deliver drugs like **opioids**, **NSAIDs**, and **anesthetics** through the skin, offering controlled, sustained release(85). These patches help maintain consistent drug levels in the bloodstream, improving efficacy while minimizing side effects such as gastrointestinal irritation(86). Bioinspired systems, such as microneedles or liposomes, enhance drug penetration and target specific pain sites, providing relief for chronic pain, post-surgical recovery, or localized pain management without the need for injections(87).

Hormone Replacement Therapy and Contraception

Bioinspired TDDS are used in **hormone replacement therapy (HRT)** and **contraception** to deliver hormones like estrogen, progesterone, or testosterone transdermally(88). These systems provide a steady release of hormones, mimicking the body's natural rhythm and reducing fluctuations often seen with oral administration(89).Bioinspired patches can improve patient compliance, reduce side effects, and offer a non-invasive alternative to oral medications, offering benefits in treating menopausal symptoms or preventing pregnancy with consistent, reliable dosing(90).

Biomimetic TDDS for Wound Healing and Dermatological Disorders

Biomimetic TDDS are used for **wound healing** and treating **dermatological disorders** by delivering therapeutic agents such as growth factors, antibiotics, or anti-inflammatory drugs directly to the affected area(91). These systems enhance skin regeneration, reduce infection risks, and promote healing by mimicking natural biological processes. Bioinspired hydrogels and nanostructures can provide sustained, localized drug release, creating optimal conditions for tissue repair while minimizing systemic side effects(92).

Advanced TDDS for Chronic Diseases (Diabetes, Hypertension, Neurodegenerative Disorders)

Bioinspired TDDS are increasingly used in managing **chronic diseases** like **diabetes**, **hypertension**, and **neurodegenerative disorders** by providing continuous, controlled release of drugs such as insulin, antihypertensives, or neuroprotective agents(93). These systems offer a non-invasive solution for long-term treatment, improving patient compliance and maintaining consistent therapeutic levels. By mimicking natural delivery mechanisms, these TDDS help manage disease progression, reduce side effects, and enhance the quality of life for patients with chronic conditions(94).

8. Challenges, Regulatory Considerations, and Market Trends

Safety, Stability, and Large-Scale Production Concerns

Safety, **stability**, and **large-scale production** are key challenges in bioinspired transdermal drug delivery systems (TDDS)(95). Ensuring the safety of new biomimetic materials involves assessing potential toxicity, skin irritation, and long-term effects(96). Stability concerns include maintaining the drug's efficacy and ensuring the integrity of the delivery system during storage and use. **Large-scale production** requires scalable manufacturing processes that preserve the quality of bioinspired TDDS, which can be costly and complex due to the need for specialized materials or precision in production(97).

Regulatory Landscape for Biomimetic Transdermal Systems (FDA, EMA Guidelines)

The **regulatory landscape** for biomimetic transdermal systems involves strict guidelines from regulatory agencies like the **FDA** (U.S.) and **EMA** (Europe)(98). Both agencies require comprehensive clinical testing to ensure the safety, efficacy, and quality of TDDS. Biomimetic systems, with their novel materials, may face additional scrutiny regarding biocompatibility, manufacturing processes, and long-term effects(99). Regulatory approvals also necessitate demonstrating consistent drug release profiles and ensuring compliance with **Good Manufacturing Practices (GMP)**, making the regulatory pathway complex but necessary for market entry(100).

Commercialization and Future Market Trends

Commercialization of bioinspired TDDS is growing as patient preference for non-invasive treatments rises(101). The market is expected to expand with advancements in **nano-medicine**, **personalized treatments**, and the increasing demand for **chronic disease management(102)**. Market trends indicate a shift towards systems that offer sustained, controlled release and target specific tissues with minimal side effects(103). Future trends also include increasing collaboration between pharmaceutical companies and technology innovators to integrate smart, responsive TDDS(104). However, high production costs and regulatory hurdles remain challenges for widespread adoption in the market(105).

9. Future Perspectives and Research Directions

Potential for AI and IoT in Biomimetic TDDS

The integration of **AI** and the **Internet of Things (IoT)** in biomimetic TDDS offers the potential for smarter, more personalized drug delivery systems(106). This synergy can improve patient compliance, optimize treatment regimens, and allow for predictive adjustments, transforming TDDS into highly adaptive, patient-centric systems(107).

Integrating Nanotechnology and Bioelectronics for Next-Gen TDDS

Nanotechnology and **bioelectronics** are poised to revolutionize TDDS by enabling the development of highly efficient, smart, and precise drug delivery systems(108). Nanomaterials like nanoparticles and nanostructured carriers can improve skin penetration and drug release control. When combined with bioelectronics, TDDS can respond dynamically to environmental cues, such as temperature or pH, to release drugs at optimal rates(109). This integration facilitates targeted delivery and the management of chronic conditions, offering a new era of advanced, responsive TDDS that can adapt to individual patient needs in real-time(110).

Ethical Considerations and Personalized Medicine Applications

The **ethical considerations** surrounding biomimetic TDDS focus on patient safety, informed consent, and the responsible use of advanced technologies(111). Ensuring that these systems are accessible, equitable, and free from biases is crucial as they become more personalized. With **personalized medicine**, TDDS can be tailored to an individual's unique biological profile, allowing for precise dosing and treatment. However, concerns related to data privacy, genetic information use, and unequal access to innovative therapies must be carefully addressed to ensure fairness and ethical standards in their implementation(112).

10. Conclusion

Summary of Key Advancements in Bioinspired and Biomimetic TDDS

Recent advancements in **bioinspired and biomimetic TDDS** include the development of **nanostructures**, **lipid-based carriers**, and **microneedle technologies** that enhance drug penetration and controlled release(113). Bioinspired **hydrogels** and **biopolymer carriers** have improved drug stability, while **responsive systems** like pH and temperature-sensitive patches offer tailored delivery(114). Innovations such as **smart TDDS** utilizing **AI** and **IoT** further refine drug administration, offering personalized and precise treatment regimens. These advancements have significantly improved the efficiency, safety, and convenience of transdermal drug delivery(115).

Impact on Patient Compliance and Therapeutic Outcomes

The bioinspired approach to **TDDS** has led to enhanced **patient compliance** by offering non-invasive, user-friendly alternatives to oral and injectable therapies(116). With sustained and controlled drug release, these systems minimize side effects and improve therapeutic outcomes(117). Patients benefit from more consistent drug levels, fewer dosing regimens, and reduced discomfort(118). As a result, these systems not only improve treatment adherence but also contribute to better clinical outcomes, particularly in chronic disease management and long-term therapies(119).

Future Challenges and Opportunities for Further Innovation

While the potential for **bioinspired TDDS** is vast, challenges remain, including ensuring **scalability**, **regulatory approval**, and **cost-effective production(120)**. Future innovations may focus on enhancing **skin penetration**, expanding the range of drugs suitable for transdermal delivery, and integrating **advanced biomaterials** for better performance(121). **Smart TDDS** incorporating AI, IoT, and nanotechnology present significant opportunities for even more personalized treatments(122). Addressing **ethical concerns** and ensuring **equitable access** will be vital for the widespread adoption of these technologies, shaping the future of transdermal drug delivery(123).

Conclusion

Bioinspired and biomimetic strategies in transdermal drug delivery systems (TDDS) represent a transformative approach to overcoming the inherent challenges posed by the skin barrier, particularly the stratum corneum, which limits the penetration of most therapeutic agents. By drawing inspiration from nature, researchers have designed innovative carriers and devices such as microneedles modeled after porcupine quills and mosquito proboscises, lipid-based vesicles mimicking cell membranes, and biopolymer-based systems utilizing chitosan, silk fibroin, and hyaluronic acid. These advancements not only enhance permeability and drug stability but also facilitate controlled, sustained, and targeted release, thereby improving patient compliance and therapeutic efficiency. Furthermore, smart and responsive systems, including pH-sensitive, enzyme-triggered, and temperature-responsive patches, offer adaptive drug release in response to physiological or environmental stimuli, paving the way for personalized and precise treatment. The integration of nanotechnology, hydrogels, and bioelectronics has further expanded the scope of TDDS, making them suitable for diverse applications such as chronic disease management, hormone replacement therapy, wound healing, and dermatological disorders. Looking ahead, the incorporation of artificial intelligence and Internet of Things technologies could revolutionize TDDS into intelligent, patient-centric systems capable of real-time monitoring and tailored drug administration. However, challenges related to large-scale manufacturing, regulatory approval, cost-effectiveness, and long-term safety remain significant barriers that must be addressed before clinical translation. Ethical considerations, particularly concerning accessibility and equitable distribution, also warrant attention to ensure that these cutting-edge technologies benefit a wide patient population. Overall, bioinspired and biomimetic TDDS hold immense potential to redefine drug delivery by providing non-invasive, efficient, and patient-friendly alternatives to conventional therapies, thereby shaping the future of modern pharmacotherapy.

Acknowledgement:

The authors are extremely thankful Raghavendra Institute of Pharmaceutical Education and Research for their extreme support and knowledge.

Conflict of Interest:

The authors declare that they have no conflict of interest.

References:

1. Baryakova TH, Pogostin BH, Langer R, McHugh KJ. Overcoming barriers to patient adherence: the case for developing innovative drug delivery systems. Nature Reviews Drug Discovery. 2023;22(5):387-409.
2. Dixit N, Maurya SD, Sagar BP. Sustained release drug delivery system. Indian Journal of Research in Pharmacy and Biotechnology. 2013;1(3):305.
3. Good WR, Lee PI. Membrane–Controlled Reservoir Drug Delivery Systems. Medical applications of controlled release: CRC Press; 2019. p. 1-40.
4. Margetts L, Sawyer R. Transdermal drug delivery: principles and opioid therapy. Continuing education in anaesthesia, critical care and pain. 2007;7(5):171-6.
5. Bajracharya R, Song JG, Back SY, Han H-K. Recent advancements in non-invasive formulations for protein drug delivery. Computational and structural biotechnology journal. 2019;17:1290-308.
6. Haque T, Talukder MMU. Chemical enhancer: a simplistic way to modulate barrier function of the stratum corneum. Advanced pharmaceutical bulletin. 2018;8(2):169.
7. Yu Y-Q, Yang X, Wu X-F, Fan Y-B. Enhancing permeation of drug molecules across the skin via delivery in nanocarriers: novel strategies for effective transdermal applications. Frontiers in bioengineering and biotechnology. 2021;9:646554.
8. Sabu C, Rejo C, Kotta S, Pramod K. Bioinspired and biomimetic systems for advanced drug and gene delivery. Journal of controlled release. 2018;287:142-55.
9. Alkilani AZ, Nasereddin J, Hamed R, Nimrawi S, Hussein G, Abo-Zour H, et al. Beneath the skin: a review of current trends and future prospects of transdermal drug delivery systems. Pharmaceutics. 2022;14(6):1152.
10. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. Nature reviews drug discovery. 2021;20(2):101-24.
11. Gao W, Hu C-MJ, Fang RH, Zhang L. Liposome-like nanostructures for drug delivery. Journal of Materials Chemistry B. 2013;1(48):6569-85.
12. Sheikhpour M, Barani L, Kasaeian A. Biomimetics in drug delivery systems: A critical review. Journal of Controlled Release. 2017;253:97-109.
13. Trucillo P. Biomaterials for drug delivery and human applications. Materials. 2024;17(2):456.
14. Yadav S, Palei NN, Dinda SC, Dhar AK. Drug Delivery in Biotechnology: Present and Future. Concepts in Pharmaceutical Biotechnology and Drug Development: Springer; 2024. p. 103-38.
15. Kang W, Xu Z, Lu H, Liu S, Li J, Ding C, et al. Advances in biomimetic nanomaterial delivery systems: harnessing nature's inspiration for targeted drug delivery. Journal of Materials Chemistry B. 2024;12(29):7001-19.
16. Wang Z, Hu W, Wang W, Xiao Y, Chen Y, Wang X. Antibacterial electrospun nanofibrous materials for wound healing. Advanced Fiber Materials. 2023;5(1):107-29.
17. Qu F, Geng R, Liu Y, Zhu J. Advanced nanocarrier-and microneedle-based transdermal drug delivery strategies for skin diseases treatment. Theranostics. 2022;12(7):3372.
18. Lamnabhi-Lagarrigue F, Annaswamy A, Engell S, Isaksson A, Khargonekar P, Murray RM, et al. Systems & control for the future of humanity, research agenda: Current and future roles, impact and grand challenges. Annual Reviews in Control. 2017;43:1-64.
19. Masloh S, Culot M, Gosselet F, Chevrel A, Scapozza L, Zeisser Labouebe M. Challenges and Opportunities in the Oral Delivery of Recombinant Biologics. Pharmaceutics. 2023;15(5):1415.

20. Gupta AK, Choudhari A, Kumar A, Kumar A, Gupta A, Faisal S, et al. Composites for drug-eluting devices: Emerging biomedical applications. Applications of biotribology in biomedical systems. 2024:251-311.
21. Schaefer H, Schalla W, Zesch A, Stüttgen G. Skin permeability: Springer Science & Business Media; 2013.
22. Yousef H, Alhajj M, Sharma S. Anatomy, skin (integument), epidermis. 2017.
23. Trommer H, Neubert R. Overcoming the stratum corneum: the modulation of skin penetration: a review. Skin pharmacology and physiology. 2006;19(2):106-21.
24. Kumar MA. The skin. Techniques in Small Animal Wound Management. 2024;1.
25. Elias PM. Lipids and the epidermal permeability barrier. Archives of Dermatological Research. 1981;270(1):95-117.
26. Eloy JO, de Souza MC, Petrilli R, Barcellos JPA, Lee RJ, Marchetti JM. Liposomes as carriers of hydrophilic small molecule drugs: strategies to enhance encapsulation and delivery. Colloids and surfaces B: Biointerfaces. 2014;123:345-63.
27. Phatale V, Vaiphei KK, Jha S, Patil D, Agrawal M, Alexander A. Overcoming skin barriers through advanced transdermal drug delivery approaches. Journal of controlled release. 2022;351:361-80.
28. Prausnitz MR, Elias PM, Franz TJ, Schmuth M, Tsai J-C, Menon GK, et al. Skin barrier and transdermal drug delivery. Dermatology. 2012;3(18):2065-73.
29. Souto EB, Fangueiro JF, Fernandes AR, Cano A, Sanchez-Lopez E, Garcia ML, et al. Physicochemical and biopharmaceutical aspects influencing skin permeation and role of SLN and NLC for skin drug delivery. Heliyon. 2022.
30. Alexander A, Dwivedi S, Giri TK, Saraf S, Saraf S, Tripathi DK. Approaches for breaking the barriers of drug permeation through transdermal drug delivery. Journal of controlled release. 2012;164(1):26-40.
31. Janse van Rensburg E. Formulation and topical delivery of liposomes and proliposomes containing clofazimine: North-West University (South Africa), Potchefstroom Campus; 2016.
32. Patel BA. Permeation enhancement and advanced strategies: A comprehensive review of improved topical drug delivery. International Research Journal of Modernization in Engineering Technology and Science. 2024;6(05):6691-702.
33. Paudel KS, Milewski M, Swadley CL, Brogden NK, Ghosh P, Stinchcomb AL. Challenges and opportunities in dermal/transdermal delivery. Therapeutic delivery. 2010;1(1):109-31.
34. Morales JO, Fathe KR, Brunaugh A, Ferrati S, Li S, Montenegro-Nicolini M, et al. Challenges and future prospects for the delivery of biologics: oral mucosal, pulmonary, and transdermal routes. The AAPS journal. 2017;19:652-68.
35. Rai VK, Mishra N, Yadav KS, Yadav NP. Nanoemulsion as pharmaceutical carrier for dermal and transdermal drug delivery: Formulation development, stability issues, basic considerations and applications. Journal of controlled release. 2018;270:203-25.
36. Brito S, Baek M, Bin B-H. Skin Structure, Physiology, and Pathology in Topical and Transdermal Drug Delivery. Pharmaceutics. 2024;16(11):1403.
37. Ramadon D, McCrudden MT, Courtenay AJ, Donnelly RF. Enhancement strategies for transdermal drug delivery systems: Current trends and applications. Drug delivery and translational research. 2021:1-34.
38. Yoo J-W, Irvine DJ, Discher DE, Mitragotri S. Bio-inspired, bioengineered and biomimetic drug delivery carriers. Nature reviews Drug discovery. 2011;10(7):521-35.
39. Zaid Alkilani A, McCrudden MT, Donnelly RF. Transdermal drug delivery: innovative pharmaceutical developments based on disruption of the barrier properties of the stratum corneum. Pharmaceutics. 2015;7(4):438-70.

40. Harun-Ur-Rashid M, Jahan I, Foyez T, Imran AB. Bio-inspired nanomaterials for micro/nanodevices: a new era in biomedical applications. Micromachines. 2023;14(9):1786.
41. McCrudden MT, McAlister E, Courtenay AJ, González-Vázquez P, Raj Singh TR, Donnelly RF. Microneedle applications in improving skin appearance. Experimental dermatology. 2015;24(8):561-6.
42. Schroeder TB, Houghtaling J, Wilts BD, Mayer M. It's not a bug, it's a feature: functional materials in insects. Advanced Materials. 2018;30(19):1705322.
43. Kim Y-C, Park J-H, Prausnitz MR. Microneedles for drug and vaccine delivery. Advanced drug delivery reviews. 2012;64(14):1547-68.
44. Zhang Z, Qian L, Zhang N, Wang X, Fu Y, Gao G, et al. Advances in Spiky Antibacterial Materials: From Bioinspired Design to Application. Small Structures. 2025;6(1):2400370.
45. Wen J, Al Gailani M, Yin N, Rashidinejad A. Liposomes and niosomes. Emulsion-based Systems for Delivery of Food Active Compounds: Formation, Application, Health and Safety. 2018:263-92.
46. Chime SA, Onyishi IV. Lipid-based drug delivery systems (LDDS): Recent advances and applications of lipids in drug delivery. Afr J Pharm Pharmacol. 2013;7(48):3034-59.
47. Tanner P, Baumann P, Enea R, Onaca O, Palivan C, Meier W. Polymeric vesicles: from drug carriers to nanoreactors and artificial organelles. Accounts of chemical research. 2011;44(10):1039-49.
48. Finbloom JA, Huynh C, Huang X, Desai TA. Bioinspired nanotopographical design of drug delivery systems. Nature Reviews Bioengineering. 2023;1(2):139-52.
49. Gomes A, Aguiar L, Ferraz R, Teixeira C, Gomes P. The emerging role of ionic liquid-based approaches for enhanced skin permeation of bioactive molecules: a snapshot of the past couple of years. International Journal of Molecular Sciences. 2021;22(21):11991.
50. Orasugh JT, Temane LT, Ray SS, Chattopadhyay D. Biopolymers for Drug Delivery. Bio-Based Polymers: Farm to Industry Volume 3: Emerging Trends and Applications: ACS Publications; 2024. p. 143-205.
51. Singh R, Shitiz K, Singh A. Chitin and chitosan: biopolymers for wound management. International wound journal. 2017;14(6):1276-89.
52. Yadav RH, Kenchegowda M, Angolkar M, Meghana T, Osmani RAM, Palaksha S, et al. A review of silk fibroin-based drug delivery systems and their applications. European Polymer Journal. 2024:113286.
53. Juncan AM, Moisă DG, Santini A, Morgovan C, Rus L-L, Vonica-Țincu AL, et al. Advantages of hyaluronic acid and its combination with other bioactive ingredients in cosmeceuticals. Molecules. 2021;26(15):4429.
54. Noreen S, Ma J-X, Saeed M, Pervaiz F, Hanif MF, Ahmed B, et al. Natural polysaccharide-based biodegradable polymeric platforms for transdermal drug delivery system: A critical analysis. Drug Delivery and Translational Research. 2022;12(11):2649-66.
55. Kotla NG, Chandrasekar B, Rooney P, Sivaraman G, Larrañaga A, Krishna KV, et al. Biomimetic lipid-based nanosystems for enhanced dermal delivery of drugs and bioactive agents. ACS Biomaterials Science & Engineering. 2017;3(7):1262-72.
56. Rauf MA. Stability and release of bioactives from liposomes. Liposomal encapsulation in food science and technology: Elsevier; 2023. p. 189-222.
57. Natsheh H, Touitou E. Phospholipid vesicles for dermal/transdermal and nasal administration of active molecules: The effect of surfactants and alcohols on the fluidity of their lipid bilayers and penetration enhancement properties. Molecules. 2020;25(13):2959.
58. Chen S, Hanning S, Falconer J, Locke M, Wen J. Recent advances in non-ionic surfactant vesicles (niosomes): Fabrication, characterization, pharmaceutical and cosmetic applications. European journal of pharmaceutics and biopharmaceutics. 2019;144:18-39.

59. Pradhan M, Srivastava S, Singh D, Saraf S, Saraf S, Singh MR. Perspectives of lipid-based drug carrier systems for transdermal delivery. Critical Reviews™ in Therapeutic Drug Carrier Systems. 2018;35(4).
60. Alvarez-Lorenzo C, Yañez-Gomez F, Concheiro A. Modular biomimetic drug delivery systems. Polymeric Biomaterials: CRC Press; 2020. p. 1027-64.
61. Yang R, Wei T, Goldberg H, Wang W, Cullion K, Kohane DS. Getting drugs across biological barriers. Advanced Materials. 2017;29(37):1606596.
62. Nasrollahi SA, Taghibiglou C, Azizi E, Farboud ES. Cell-penetrating peptides as a novel transdermal drug delivery system. Chemical biology & drug design. 2012;80(5):639-46.
63. Bruno BJ, Miller GD, Lim CS. Basics and recent advances in peptide and protein drug delivery. Therapeutic delivery. 2013;4(11):1443-67.
64. Jacob S, Nair AB, Shah J, Sreeharsha N, Gupta S, Shinu P. Emerging role of hydrogels in drug delivery systems, tissue engineering and wound management. Pharmaceutics. 2021;13(3):357.
65. Gyles DA, Castro LD, Silva Jr JOC, Ribeiro-Costa RM. A review of the designs and prominent biomedical advances of natural and synthetic hydrogel formulations. European Polymer Journal. 2017;88:373-92.
66. Zelikin AN, Ehrhardt C, Healy AM. Materials and methods for delivery of biological drugs. Nature chemistry. 2016;8(11):997-1007.
67. Peppas NA, Bures P, Leobandung W, Ichikawa H. Hydrogels in pharmaceutical formulations. European journal of pharmaceutics and biopharmaceutics. 2000;50(1):27-46.
68. Wong YL, Pandey M, Choudhury H, Lim WM, Bhattamisra SK, Gorain B. Development of in-situ spray for local delivery of antibacterial drug for Hidradenitis suppurativa: investigation of alternative formulation. Polymers. 2021;13(16):2770.
69. Pham H-P, Vo V-T, Nguyen T-Q. Optimizing CNC milling parameters for manufacturing of ultra-sharp tip microneedle with various tip angles. Drug Delivery and Translational Research. 2024:1-17.
70. Rojekar S, Parit S, Gholap AD, Manchare A, Nangare SN, Hatvate N, et al. Revolutionizing Eye Care: Exploring the Potential of Microneedle Drug Delivery. Pharmaceutics. 2024;16(11):1398.
71. Raikar AS, Kalaskar D, Bhilegaonkar S, Somnache SN, Bodaghi M. Revolutionizing drug delivery by bioinspired 4D transdermal microneedles: Advances and future horizons. European Polymer Journal. 2024:112952.
72. McGill S. Low back disorders: evidence-based prevention and rehabilitation: Human Kinetics; 2015.
73. Kumar D, Pandey S, Shiekmydeen J, Kumar M, Chopra S, Bhatia A. Therapeutic Potential of Microneedle Assisted Drug Delivery for Wound Healing: Current State of the Art, Challenges, and Future Perspective. AAPS PharmSciTech. 2025;26(1):1-29.
74. Xiu X, Gao G, Liu Y, Ma F. Drug delivery with dissolving microneedles: Skin puncture, its influencing factors and improvement strategies. Journal of Drug Delivery Science and Technology. 2022;76:103653.
75. Tsioris K, Raja WK, Pritchard EM, Panilaitis B, Kaplan DL, Omenetto FG. Fabrication of silk microneedles for controlled-release drug delivery. Advanced Functional Materials. 2012;22(2):330-5.
76. Wang M, Hong Y, Fu X, Sun X. Advances and applications of biomimetic biomaterials for endogenous skin regeneration. Bioactive Materials. 2024;39:492-520.
77. Rizwan M, Yahya R, Hassan A, Yar M, Azzahari AD, Selvanathan V, et al. pH sensitive hydrogels in drug delivery: Brief history, properties, swelling, and release mechanism, material selection and applications. Polymers. 2017;9(4):137.

78. Zhang X, Chen G, Zhang H, Shang L, Zhao Y. Bioinspired oral delivery devices. Nature Reviews Bioengineering. 2023;1(3):208-25.
79. Balaure PC, Gudovan D, Gudovan IA. Smart triggered release in controlled drug delivery. Current Drug Targets. 2018;19(4):318-27.
80. Hu Q, Katti PS, Gu Z. Enzyme-responsive nanomaterials for controlled drug delivery. Nanoscale. 2014;6(21):12273-86.
81. Neubi GMN, Opoku-Damoah Y, Gu X, Han Y, Zhou J, Ding Y. Bio-inspired drug delivery systems: an emerging platform for targeted cancer therapy. Biomaterials science. 2018;6(5):958-73.
82. Sharma KS. Artificial intelligence assisted fabrication of 3D, 4D and 5D printed formulations or devices for drug delivery. Current drug delivery. 2023;20(6):752-69.
83. Reichert S, Menges A, Correa D. Meteorosensitive architecture: Biomimetic building skins based on materially embedded and hygroscopically enabled responsiveness. Computer-Aided Design. 2015;60:50-69.
84. Mariello M, Eş I, Proctor CM. Soft and flexible bioelectronic micro-systems for electronically controlled drug delivery. Advanced Healthcare Materials. 2024;13(24):2302969.
85. Babaie S, Taghvimi A, Hong J-H, Hamishehkar H, An S, Kim KH. Recent advances in pain management based on nanoparticle technologies. Journal of Nanobiotechnology. 2022;20(1):290.
86. Filho D, Guerrero M, Pariguana M, Marican A, Durán-Lara EF. Hydrogel-Based Microneedle as a Drug Delivery System. Pharmaceutics. 2023;15(10):2444.
87. Chen G, Wang X, Li J, Xu Y, Lin Y, Wang F. Intelligent hydrogels for treating malignant melanoma. Engineered Regeneration. 2024.
88. Lunter D, Klang V, Eichner A, Savic SM, Savic S, Lian G, et al. Progress in Topical and Transdermal Drug Delivery Research—Focus on Nanoformulations. Pharmaceutics. 2024;16(6):817.
89. Ohdo S. Chronotherapeutic strategy: rhythm monitoring, manipulation and disruption. Advanced drug delivery reviews. 2010;62(9-10):859-75.
90. Hwang I, Kim HN, Seong M, Lee SH, Kang M, Yi H, et al. Multifunctional smart skin adhesive patches for advanced health care. Advanced healthcare materials. 2018;7(15):1800275.
91. Shende SM, Khapne AK. EXPLORING THE EVOLUTION OF PATCHES AND IMPACT OF SMART PATCHES ON DRUG DELIVERY: A COMPREHENSIVE REVIEW.
92. Ren Y, Chen C, Zhang M, Ding X, Zhang L, Jiang X, et al. Application of nanostructure-loaded hydrogels for cancer treatment and tissue regeneration. Applied Materials Today. 2024;37:102086.
93. Narayanan KB, Bhaskar R, Han SS. Recent advances in the biomedical applications of functionalized nanogels. Pharmaceutics. 2022;14(12):2832.
94. Bhardwaj H, Khute S, Sahu R, Jangde RK. Advanced drug delivery system for management of chronic diabetes wound healing. Current Drug Targets. 2023;24(16):1239-59.
95. Dalvi M, Kharat P, Thakor P, Bhavana V, Singh SB, Mehra NK. Panorama of dissolving microneedles for transdermal drug delivery. Life Sciences. 2021;284:119877.
96. Singh AV, Chandrasekar V, Prabhu VM, Bhadra J, Laux P, Bhardwaj P, et al. Sustainable bioinspired materials for regenerative medicine: balancing toxicology, environmental impact, and ethical considerations. Biomedical Materials. 2024;19(6):060501.
97. Saud A, Gupta S, Allal A, Preud'Homme H, Shomar B, Zaidi SJ. Progress in the sustainable development of biobased (nano) materials for application in water treatment technologies. ACS omega. 2024;9(27):29088-113.

98. Godoi MM, Reis EM, Koepp J, Ferreira J. Perspective from developers: Tissue-engineered products for skin wound healing. International Journal of Pharmaceutics. 2024:124319.
99. Tripathi D, Pandey P, Sharma S, Rai AK, BH MP. Advances in nanomaterials for precision drug delivery: Insights into pharmacokinetics and toxicity. BioImpacts. 2024;15(1):30573-.
100. Hock SC, Kian SM, Wah CL. Global challenges in the manufacture, regulation and international harmonization of GMP and quality standards for biopharmaceuticals. Generics and Biosimilars Initiative Journal. 2020;9(2):52-64.
101. Al-Nimry SS, Daghmash RM. Three dimensional printing and its applications focusing on microneedles for drug delivery. Pharmaceutics. 2023;15(6):1597.
102. Mitra S, Singh PK, Mohapatra RK, Mohapatra NP, Sarkar B, Mishra S. A Perspective on the Global Market of Micro-and Nano-Smart Materials in Pharmaceutical Industries. Smart Micro-and Nanomaterials for Pharmaceutical Applications: CRC Press. p. 17-38.
103. Yun YH, Lee BK, Park K. Controlled Drug Delivery: Historical perspective for the next generation. Journal of Controlled Release. 2015;219:2-7.
104. Fucà R, Cubico S, Leitão J, Favretto G, Ardolino P. Post-COVID-19 Advancing Targeted Drug Delivery (TDD): Literature Insights and Market Dynamics. Emerging Social Issues on Targeted Drug Delivery. 2024;255.
105. Tofail SA, Koumoulos EP, Bandyopadhyay A, Bose S, O'Donoghue L, Charitidis C. Additive manufacturing: scientific and technological challenges, market uptake and opportunities. Materials today. 2018;21(1):22-37.
106. Murthy H, Zurek-Mortka M, Pillai VJ, Kumar KP. Internet of Things in Bioelectronics: Emerging Technologies and Applications. 2024.
107. Singh M, Kumar A, Khanna NN, Laird JR, Nicolaides A, Faa G, et al. Personalized Medicine for Cardiovascular Disease Risk in Artificial Intelligence Framework. 2023.
108. Soni A, Singh P, Tripathi GK, Dixit P. IoT and Nano-Bioelectronics for Target Drug Delivery. Internet of Things in Bioelectronics: Emerging Technologies and Applications. 2024:17-40.
109. Rahimnejad M, Jahangiri S, Zirak Hassan Kiadeh S, Rezvaninejad S, Ahmadi Z, Ahmadi S, et al. Stimuli-responsive biomaterials: smart avenue toward 4D bioprinting. Critical reviews in biotechnology. 2024;44(5):860-91.
110. Laurn P, Arean M. Advances in Transdermal Drug Delivery Systems for Systemic Disease Management. Journal of Advanced Pharmaceutical Research Sciences and Sustainability (JAPRSS). 2024;1(1):1-12.
111. Turini S. Nanomolecular Electromagnetic Interference Agents in Biological Systems: Unraveling the Mechanisms and Implications for Future Biowarfare Strategies. 2024.
112. Fusar-Poli P, Manchia M, Koutsouleris N, Leslie D, Woopen C, Calkins ME, et al. Ethical considerations for precision psychiatry: a roadmap for research and clinical practice. European Neuropsychopharmacology. 2022;63:17-34.
113. Chen Q, Yang Z, Liu H, Man J, Oladejo AO, Ibrahim S, et al. Novel Drug Delivery Systems: An Important Direction for Drug Innovation Research and Development. Pharmaceutics. 2024;16(5):674.
114. Luo J, Zhao X, Guo B, Han Y. Preparation, thermal response mechanisms and biomedical applications of thermosensitive hydrogels for drug delivery. Expert Opinion on Drug Delivery. 2023;20(5):641-72.
115. Prajapati VD, Shrivastav P, Suthar K. Controlled Drug Delivery Systems: Concepts and Rationale. Novel Drug Delivery Systems (Part 1). 2024:1.

116. Jose J, Rodrigues IS, Preetha H, Konkody K. Recent Progress of Transdermal Drug Delivery Systems for Biomedical Applications. Modeling and Control of Drug Delivery Systems. 2021:111-23.
117. Senapati S, Mahanta AK, Kumar S, Maiti P. Controlled drug delivery vehicles for cancer treatment and their performance. Signal transduction and targeted therapy. 2018;3(1):7.
118. Grass JA. Patient-controlled analgesia. Anesthesia & Analgesia. 2005;101(5S):S44-S61.
119. Burnier M. The role of adherence in patients with chronic diseases. European journal of internal medicine. 2024;119:1-5.
120. Balakrishnan P, Gopi S. Revolutionizing transdermal drug delivery: unveiling the potential of cubosomes and ethosomes. Journal of Materials Chemistry B. 2024;12(18):4335-60.
121. Chatterjee P, Dhibar S. Nanomaterial marvels: Pioneering applications and cutting-edge advancements in drug delivery. Nano and Medical Materials. 2023;3(2):220.
122. Heydari S, Masoumi N, Esmaeeli E, Ayyoubzadeh SM, Ghorbani-Bidkorpeh F, Ahmadi M. Artificial intelligence in nanotechnology for treatment of diseases. Journal of Drug Targeting. 2024;32(10):1247-66.
123. Stasevych M, Zvarych V. Innovative robotic technologies and artificial intelligence in pharmacy and medicine: paving the way for the future of health care—a review. Big Data and Cognitive Computing. 2023;7(3):147.