International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 04-08-2026, Accepted: 03-09-2026, Published: 18-09-2026
Volume 11, Issue 3, 2026, Page No. 95-102

A review on "artificial intelligence in transdermal drug delivery systems: Current advances, challenges, and future perspectives."

Panthagada Sunitha[1*], Devaguptapu Pujitha[2], Dasari Hemima[2], Kamuju Navya Sri[2], Vasa Bhanu Durga[2], Abbadasari Uday[2]

[1] Associate Professor, Department of Pharmaceutical Analysis, Koringa College of Pharmacy, Korangi Kakinada, Andhra Pradesh, India

[2] Koringa College of Pharmacy, Korangi, Kakinada, Andhra Pradesh, India

Corresponding Author: Panthagada Sunitha

DOI: https://doi.org/10.66856/ijrpps.2026.11.3.11085

Abstract

Transdermal drug delivery systems (TDDS) provide an alternative to traditional oral and injectable routes by delivering drugs through the skin, thereby avoiding the gastrointestinal tract and first-pass liver metabolism, enhancing bioavailability, and reducing systemic adverse effects. Recent developments in artificial intelligence (AI) have created new opportunities to address existing challenges and accelerate the development of transdermal drug delivery systems (TDDS). This review emphasizes the growing importance of AI in the design, optimization, and assessment of TDDS. Advanced machine learning and deep learning techniques, such as artificial neural networks, quantitative structure–activity relationship (QSAR) models, ensemble learning, and physiologically based pharmacokinetic modelling, show considerable promise in predicting skin permeability, drug diffusion, formulation efficiency, and pharmacokinetic responses. Furthermore, AI-based approaches facilitate the rapid screening of drug candidates and the optimization of polymer matrices, permeation enhancers, and adhesive systems, thereby reducing dependence on conventional trial-and-error experimentation.

Keywords: Patches, drug delivery, permeation, technology, skin

Introduction

1. Artificial Intelligence

Over the past several decades, artificial intelligence has evolved from a theoretical concept into practical technologies that are now widely used in everyday life. The term "artificial intelligence" was first formally introduced during the Dartmouth conference in 1956 [1]. Since its early development, artificial intelligence has progressed considerably, moving from basic rule-based programs and expert systems to sophisticated techniques such as machine learning and deep learning. These modern approaches enable computers to process large datasets, recognize complex patterns, and generate insights with minimal human intervention [2].

2. History of Artificial Intelligence

Artificial intelligence emerged as a formal field of study following a 1956 workshop at Dartmouth College. [3]1955 – Allen Newell and Herbert A. Simon developed one of the earliest artificial intelligence programs, known as the Logic Theorist. The program successfully demonstrated 38 of the 52 mathematical theorems and also discovered new, more elegant proofs for several of them [4].

- In 2011, IBM's Watson made history by winning Jeopardy, a popular quiz show that challenged it witdifficult questions and word puzzles. Its victory demonstrated that Watson could interpret natural language and respond to complex questions with impressive speed and accuracy [5].
- In 2012, Google introduced the "Google Now" feature for Android, which could anticipate users' needs and provide relevant information proactively [6].
- The advancement of deep learning during the 2000s, along with the emergence of Deep QA in 2007, significantly expanded the use of artificial intelligence in healthcare. Later, in 2010, computer-aided detection (CAD) was used in endoscopy for the first time, marking another important step in the application of AI to medical diagnosis [7].

3. The Role of AI in Drug Delivery System

A focused review of existing research examined recent developments in combining artificial intelligence (AI) with drug delivery systems and nanotechnology [8]. The emergence of nanotechnology marked a significant advancement in medicine, making it possible to create advanced drug delivery systems (DDS), including liposomes, polymer-based nanoparticles, and dendrimers [9]. Artificial intelligence is increasingly being applied to enhance drug development efficiency and lower associated costs focused review of existing research examined recent developments in combining artificial intelligence (AI) with drug delivery systems and nanotechnology [8]. The emergence of nanotechnology marked a significant advancement in medicine, making it possible to create advanced drug delivery systems (DDS), including liposomes, polymer-based nanoparticles, and dendrimers [9]. Artificial intelligence is increasingly being applied to enhance drug development efficiency and lower associated costs through predictive modeling of drug delivery systems. These computational approaches assist in optimizing drug–excipient combinations and formulations, helping to ensure that therapeutic agents are effectively delivered to their intended sites of action within the body [10].

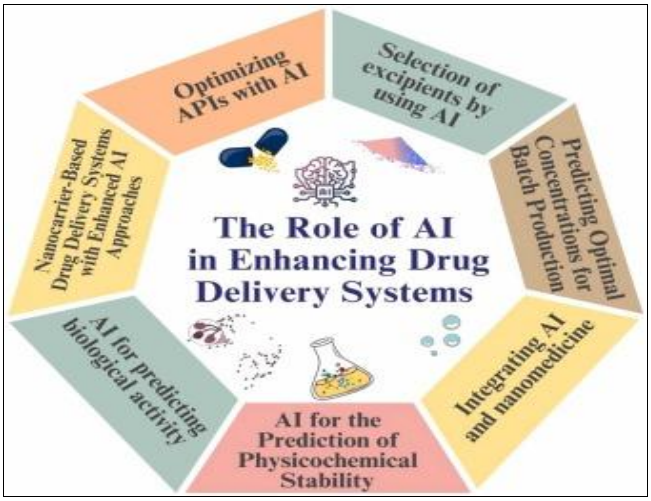

Fig 1: The role of AI in enhancing drug delivery system

Selection of Excipients by Using AI

Choosing suitable excipients is an essential part of pharmaceutical formulation development, as it strongly influences formulation stability, solubility, ease of manufacturing, bioavailability, and patient acceptance. Conventional excipient selection has mainly relied on experimental screening, existing knowledge, and pharmacopeial recommendations. However, this conventional strategy can be labor-intensive and costly, while also being insufficient for accurately identifying the complex and nonlinear interactions that may occur between active pharmaceutical ingredients (APIs) and excipients [11]. Artificial intelligence, particularly machine learning algorithms, supports well-informed decision-making during the early stages of formulation development by identifying complex, non-linear relationships among multiple formulation parameters and the target product characteristics [12]. Artificial intelligence has shown considerable potential in predicting drug–excipient interactions, which play a vital role in pre-formulation studies. Detecting possible incompatibilities at an early stage helps prevent degradation, loss of therapeutic efficacy, and alterations in drug bioavailability [13].

Principles for Transdermal Drug Delivery System

Transdermal drug delivery systems (TDDS), also referred to as transdermal patches, are pharmaceutical dosage forms developed to administer a therapeutically effective amount of drug across the skin for systemic absorption [14]. The oral route is widely regarded as the most preferred, convenient, and practical method of drug administration because of its numerous benefits. However, it also has several limitations, including enzymatic degradation in the gastrointestinal tract, gastrointestinal irritation, poor absorption, and reduced bioavailability. Additionally, some medications are not suitable or safe for oral administration. When drugs must be given through the parenteral route, patients may experience needle phobia, particularly children and some adults, and there is also a risk of infection associated with the injection process [15]. To address the limitations of oral and parenteral drug delivery, the transdermal drug delivery system (TDDS) has emerged as an effective alternative for suitable drugs.

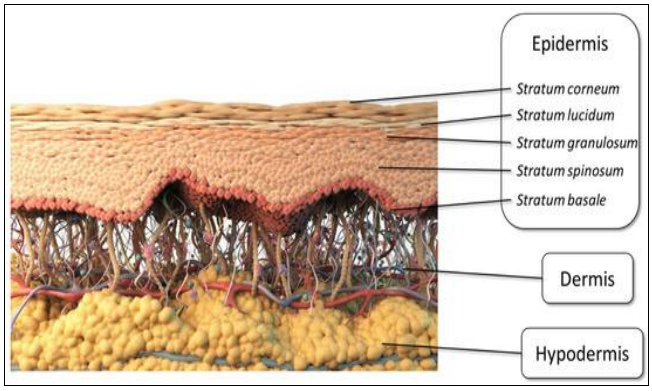

Fig 2: Layers of the Skin

The skin serves as the body's primary protective barrier, shielding it from harmful substances, pathogens, and environmental contaminants. The outermost layer, the stratum corneum (approximately 15 µm thick), consists of keratinocytes embedded in a lipid matrix that forms a strong barrier to drug penetration. [16] The skin's limited permeability hinders the transport of large and hydrophilic molecules, making it necessary to employ penetration enhancers, advanced drug delivery systems, or chemical modification strategies to improve drug absorption [17]

In addition, the formulation of effective transdermal drug delivery systems (TDDS) is challenging, as it requires careful optimization of drug stability, controlled drug release, and compatibility with the physiological properties of the skin. Over the last decade, significant progress has been made in TDDS research, leading to the development of advanced technologies and a growing number of scientific publications. This increasing research activity reflects global efforts to address key challenges such as the limited permeability of the skin and the effective delivery of macromolecular drugs. Innovative approaches, including microneedles, chemical penetration enhancers (CPEs), and nanotechnology-based delivery systems, have received considerable attention. Among these, microneedle technology has emerged as a promising strategy and has been widely investigated for applications such as vaccine administration, pain management, and enhanced transdermal drug delivery [18, 19].

Nanocarrier-based systems, including liposomes and nanoparticles, enhance drug stability and facilitate targeted drug delivery, particularly in cancer therapy and dermatological applications. Physical enhancement techniques such as electroporation and photomechanical waves temporarily increase skin permeability by disrupting the skin barrier, thereby improving the transport of therapeutic molecules. Similarly, thermal ablation uses controlled localized heat to create temporary microchannels in the skin, enhancing drug penetration and enabling rapid, site-specific drug delivery [18, 19]

Transdermal drug delivery (TDD) is an effective alternative to conventional drug administration because it bypasses first-pass hepatic metabolism and enables sustained drug release over an extended period. In addition, it is a non-invasive and painless approach, improving patient comfort and compliance compared with injectable formulations. Despite these advantages, the skin functions as the body's primary protective barrier, defending against harmful microorganisms, toxins, and environmental contaminants.

The outermost skin layer, known as the stratum corneum (approximately 15 μ m thick), consists of keratinocytes embedded within a lipid-rich matrix that forms a highly organized structure. This unique architecture provides very low permeability to foreign molecules, making the stratum corneum the principal barrier to transdermal drug transport and limiting the penetration of many therapeutic agents [22]

How AI Works with Transdermal Drug Delivery System

Artificial intelligence (AI) has emerged as a valuable tool for improving transdermal drug delivery systems (TDDS) by supporting the design, optimization, and personalization of pharmaceutical patches. Through the application of machine learning algorithms and predictive modeling, AI can evaluate extensive datasets containing information on drug properties, polymer characteristics, and skin permeability to determine the most effective formulation [23]. Artificial intelligence (AI) accelerates the drug development process by identifying potential drug candidates that are appropriate for transdermal administration. It also improves manufacturing efficiency by enabling automated quality assurance and maintaining product consistency. In addition, AI supports regulatory decision-making through the analysis of clinical trial data, ensuring compliance with established standards. Overall, the integration of AI enhances the efficiency, precision, and patient-centered nature of transdermal drug delivery systems [24]

1. Ai In Drug Delivery

Deep learning, a specialized branch of artificial intelligence based on multilayer neural networks, employs several hidden layers to process complex data and automatically extract meaningful features. Modern deep learning models, including generative adversarial networks (GANs), recurrent neural networks (RNNs), and transfer learning approaches, have been widely adopted in healthcare for applications such as small-molecule drug design and aging-related studies [25]. Researchers developed a deep learning model that combined genomic and proteomic features to predict human genes associated with a range of age-related diseases [26].

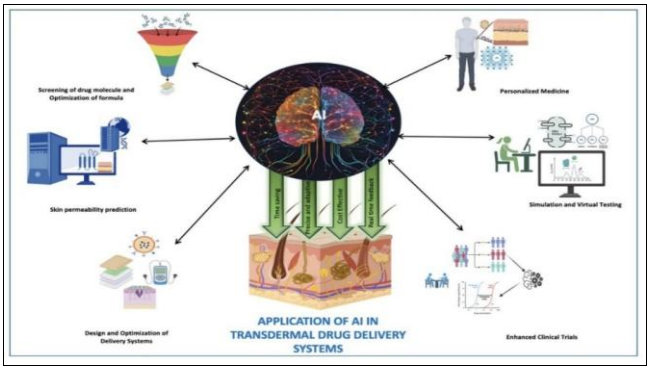

Fig 3: Application of AI in transdermal drug delivery systems

2. AI IN Modeling Skin Permeation and Diffusion

The extensive application of TDDS remains limited due to the skin's permeability barrier, mainly the stratum corneum, and the necessity for optimized drug formulations [27]. The poor permeability of the skin prevents the efficient passage of large and hydrophilic compounds, requiring the application of penetration enhancers, sophisticated delivery systems, or chemical alteration of the drug molecule [28].

This study uses AI-based methods to estimate the skin permeability (Log K p) of FDA-approved drugs from their molecular structures, employing regression and clustering approaches to identify permeability trends and support the selection of suitable candidates for transdermal drug delivery [29]. Development of AI-based models to estimate the skin permeability (Log K p) of FDA-approved drugs using their molecular structures [30].

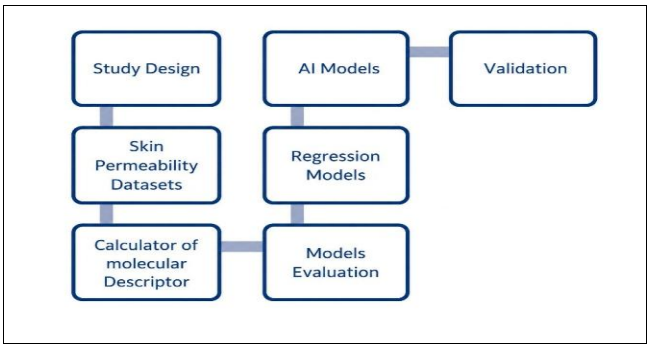

Fig 4: showing AI in modeling skin permeation and diffusion.

TDDS For the Treatment of Viral Infections

Artificial intelligence and machine learning (ML) technologies enable the extraction of valuable information, providing practical insights that support accurate disease diagnosis and the development of optimized pharmaceutical formulations [31]. The application of advanced drug delivery strategies using novel nanocarriers aims to transport therapeutic agents directly to the target site, thereby achieving a more substantial reduction in viral load compared with conventional dosage forms [32]. Recent research indicates that transdermal administration may serve as a promising alternative approach for delivering COVID-19 vaccines [33]. A comparative investigation evaluated binary ethanolic lipid vesicles (ETHOs) and elastic liposomes (ELPs) as transdermal carriers for the delivery of sodium acyclovir (ACV-Na) [34]. Influenza vaccine-loaded egg microneedles (FLU-EMN) were developed and evaluated, demonstrating their potential as an efficient and minimally invasive drug delivery system that eliminates the requirement for cold storage [35]. For autoimmune diseases such as rheumatoid arthritis and psoriasis, transdermal drug delivery systems (TDDS) have been investigated as a means of administering ati-inflammatory and immunosuppressive agents directly to the affected sites, thereby reducing systemic adverse effects [36]. Machine learning enhances microneedle design by optimizing critical parameters, including needle length, tip geometry, and material composition, to improve delivery efficiency while reducing patient discomfort [37].

1. TDDS for the Treatment of Autoimmune Disorders

- Transdermal drug delivery systems (TDDS) have demonstrated significant potential in the treatment of hormonal disorders and autoimmune diseases. In the management of hormonal imbalances, TDDS provides an efficient approach for delivering hormones such as estrogen, testosterone, and progesterone, commonly through patches or gel-based formulations [38].
- Hormone replacement therapy (HRT) frequently utilizes transdermal patches to manage menopausal

symptoms in women and treat androgen deficiency in men [39].

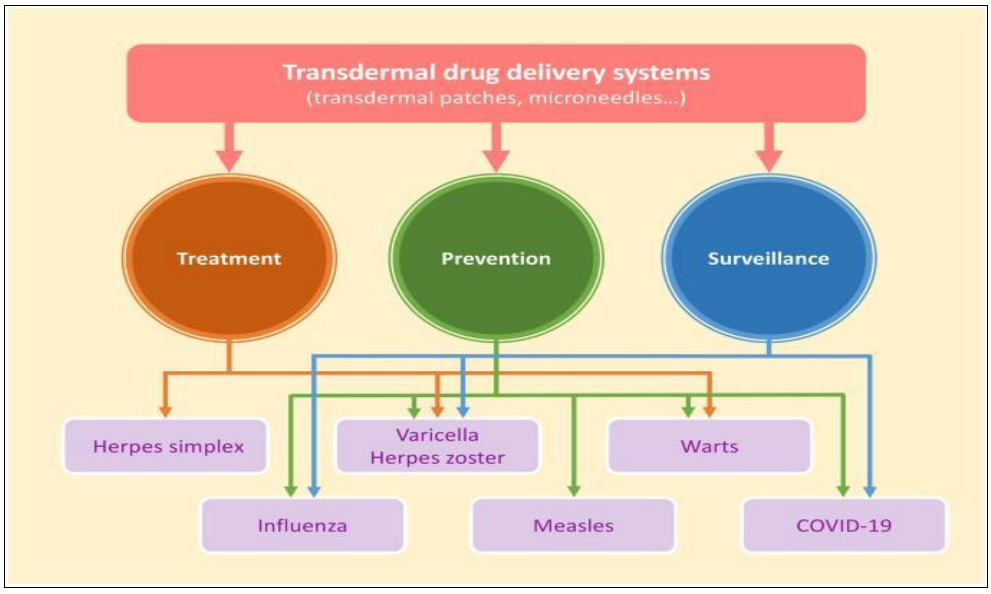

Fig 5: Transdermal drug delivery systems

2. TDDS for the Treatment of Cardiovascular Diseases

- Transdermal patch delivery systems can serve as an efficient alternative for administering drugs. Propranolol, a nonselective beta-adrenergic receptor blocker, experiences extensive first-pass hepatic metabolism following oral administration, resulting in an oral bioavailability of approximately 23% [40].
- Clonidine, an α2-adrenergic receptor agonist, is another antihypertensive medication that has been formulated for transdermal patch administration. It was originally developed and introduced for the management of hypertension [41].
- Nitroglycerin-derived nitric oxide (NO) promotes relaxation of vascular smooth muscle by stimulating the production of cyclic guanosine monophosphate (cGMP), resulting in vasodilation [42].
- A comparative evaluation of edematous and non-edematous patients treated with the Bisono® Tape 4 mg patch demonstrated C max values of 13.3 ng/mL in the edema group and 17 ng/mL in the non-edema group [43].

3. TDDS for the Treatment of Central Nervous System Disorders

- Transdermal drug delivery systems containing nicotinic agonists, especially nicotine, are widely utilized to support smoking cessation and alleviate withdrawal symptoms [44].
- The effectiveness of transdermal buprenorphine therapy in controlling severe chronic pain associated with conditions such as cancer may help reduce the reliance on oral pain medications [45].
- Transdermal rivastigmine has been effective in reducing cognitive and functional impairments in patients with Alzheimer's disease [46].
- A transdermal delivery system incorporating the antidepressant selegiline, which effectively inhibits the central monoamine oxidase A (MAO-A) and monoamine oxidase B (MAO-B) enzymes [47].

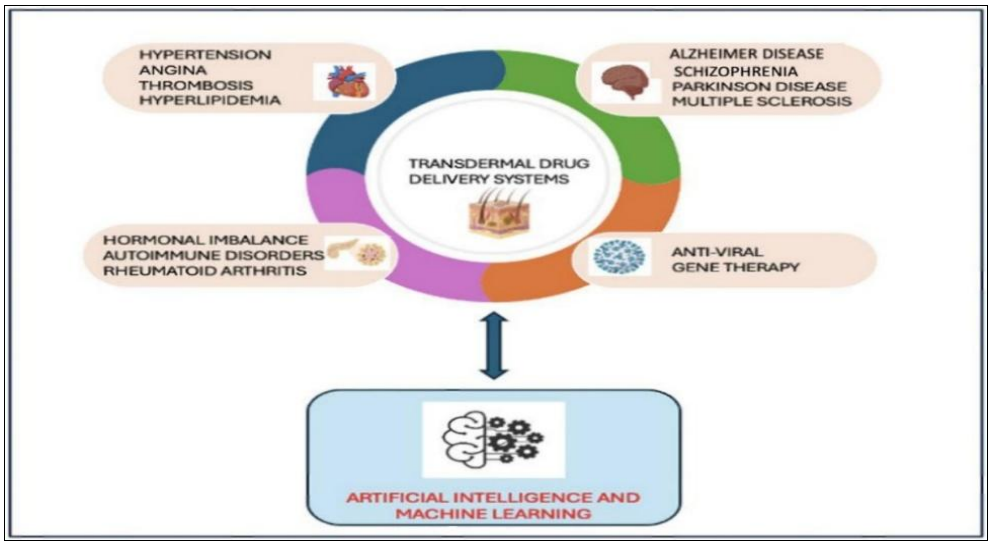

Fig 6: Integration of AI and MLTDDS-based therapies.

Personalized Therapy Through Smart Patches

- A transdermal or skin patch is an adhesive medicated system applied to the skin to administer a predetermined amount of medicine into the bloodstream. It may also support the healing of an affected or injured body area. Compared with other routes of drug administration, such as oral or topical delivery, the transdermal route offers the important benefit of providing a controlled and continuous release of the medication to the patient [48].
- Transdermal administration of large proteins represents an innovative and promising approach to drug delivery, as no commercially available transdermal patch technology currently enables the incorporation of proteins [49]
- In premenopausal women, the estimated daily production of testosterone is about 300 µ g, with nearly equal contributions from the ovaries and adrenal glands. Women experiencing spontaneous premature ovarian failure (s POF) at a young age may exhibit reduced androgen concentrations compared with women who have normal ovulatory function. The testosterone transdermal patch (TTP) was developed to mimic the natural rate of testosterone secretion by the ovaries. When TTP was combined with cyclic E2/MPA therapy in women with s POF, the average free testosterone concentrations reached levels close to the upper boundary of the normal range [50]
- Transdermal patch technology is widely used to provide pain relief. While the Duragesic patch is well known, several other patches are also available, including Lidoderm, which contains 5% lidocaine and is commonly prescribed for managing postherpetic neuralgia [51]
- This medication is an oxybutynin hydrochloride transdermal patch marketed as Oxybutynin in the United States and Kenter in Europe. Oxybutynin is a transparent, thin, and flexible patch designed for application to the abdomen, hip, or buttock twice a week, ensuring a steady and continuous release of oxybutynin for approximately three to four days [52]

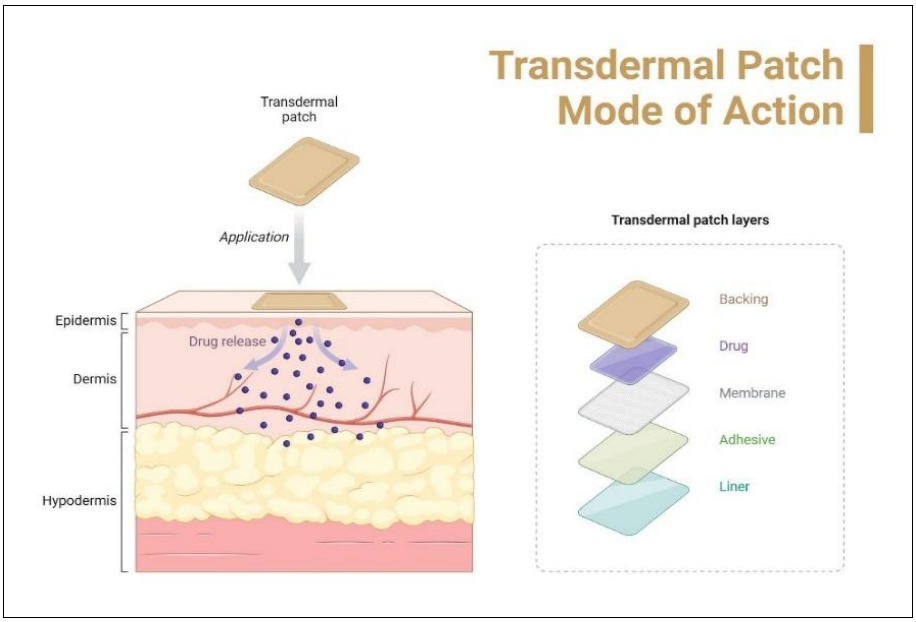

Fig 7: Application of Transdermal patches

Applications for Transdermal Drug Delivery System

- TDDS is highly effective for the topical treatment of cutaneous viral infections, as it reduces systemic drug absorption and minimizes adverse effects that are often associated with oral or subcutaneous drug administration [53]
- Tetracyclines are broad-spectrum antibiotics widely valued in dermatology, and over the last decade, their clinical applications have expanded to treat a diverse range of skin conditions [54].
- Artificial intelligence models can evaluate extensive datasets on the skin permeability of different compounds to determine their potential for transdermal drug delivery. These models can also optimize formulations by considering factors such as skin type, hydration status, and the intended drug. In a study by Abdallah et al., AI-based regression and clustering methods were used to predict the skin permeability (Log Kp) of FDA-approved drugs from their molecular structures, helping identify suitable candidates for transdermal formulations [55]
- Artificial intelligence plays an important role in improving the development and optimization of transdermal patches by evaluating factors such as patch geometry, adhesive characteristics, and material composition [56]

Future Potential of AI in Overcoming Obstacles in TDDS

The integration of artificial intelligence (AI) into transdermal drug delivery systems (TDDS) is likely to transform both therapeutic development and clinical applications. AI-enabled smart patches equipped with biosensors could continuously track physiological indicators, including glucose concentration, temperature, and skin hydration, and use this information to adjust drug

release dynamically. Furthermore, AI-driven personalization may improve transdermal treatment by incorporating individual factors such as age, genetic characteristics, skin properties, and metabolic status to optimize drug formulations and dosing schedules. In addition, AI-supported virtual clinical trials and digital twin models could predict patient responses more efficiently, potentially accelerating drug development while reducing the need for extensive animal and in vivo studies. Another promising advancement is the development of electronic TDDS patches that can monitor biomarkers and deliver two different drugs at controlled rates. One example is a closed-loop insulin and glucagon patch designed for automated diabetes management. Future research may also focus on improving micro needle-based drug delivery systems to minimize skin damage, enhance safety, and reduce manufacturing costs.

References

1. Samuel AL. Some Studies in Machine Learning Using the Game of Checkers. IBM J. Res. Dev.,1959:3(3):210–229.
2. LeCun Y, Bottou L, Bengio Y, Haffner P. Gradient-based learning applied to document recognition. Proc. IEEE,2002:86(11):2278–2324.
3. Kaplan A, Haenlein M. Siri, Siri in my Hand, who's the Fairest in the Land? On the Interpretations, Illustrations and Implications of Artificial Intelligence. Business Horizons,2018:62:15–25.
4. Schwab A, Friend S. Artificial intelligence and drug discovery. Trends in Biotechnology,2018:36(7):694–704.
5. Choudhury A, Das D. Applications of artificial intelligence in healthcare operations management, A review of the literature and future directions. Computers & Industrial Engineering,2020:145:106457.
6. Rajkomar A, Dean J, Kohane I. Machine learning in medicine. New England Journal of Medicine,2019:380(14):1347–1358.
7. Srinivasan S, Hossain M, Lopez A. Artificial intelligence in drug development, Present status and future prospects. Drug Discovery Today,2019:24(3):773–780.
8. Alizadehsani R, Oyelere SS, Hussain S, Jagatheesaperumal SK, Calixto RR, Rahouti M, Roshanzamir M, De Albuquerque VH. Explainable artificial intelligence for drug discovery and development, a comprehensive survey. IEEE Access,2024:12:35796–35812.
9. Wilhelm S, Tavares AJ, Dai Q, Ohta S, Audet J, Dvorak HF, et al. Analysis of nanoparticle delivery to tumours. Nature Reviews Materials,2016:1(5):16014.
10. Krauss JK, Lipsman N, Aziz T, Boutet A, Brown P, Chang JW, Davidson B, Grill WM, Hariz MI, Horn A, Schulder. Technology of deep brain stimulation, current status and future directions. Nature Reviews Neurology,2021:17(2):75–87.
11. Mak KK, Pichika MR. Artificial intelligence in drug development, Present status and future prospects. Drug Discovery Today,2019:24:773–780. Doi: 10.1016/j.drudis.2018.11.014.
12. Galata DL, Könyves Z, Nagy B, Novák M, Mészáros LA, Szabó E, et al. Real-time release testing of dissolution based on surrogate models developed by machine learning algorithms using NIR spectra, compression force and particle size distribution as input data. International Journal of Pharmaceutics,2021:597:120338.
13. Rastogi V, Yadav P. Transdermal drug delivery system, An Overview. Asian Journal of Pharmaceutics,2010:6:161.
14. Chunara H. Transdermal drug delivery system, An overview. Asian Journal of Pharmaceutics, 2012.
15. Karande P, Mitragotri S. Enhancement of transdermal drug delivery via synergistic action of chemicals. Biochimica et Biophysica Acta,2009:1788(11):2362–2373.
16. Herman A, Herman AP. Essential oils and their constituents as skin penetration enhancer for transdermal drug delivery, a review. Journal of Pharmacy and Pharmacology,2015:67(4):473–485.
17. Matharoo N, Mohd H, Michniak-Kohn B. Transferosomes as a transdermal drug delivery system, Dermal kinetics and recent Developments. Wiley Interdisciplinary Reviews Nanomedicine and Nanobiotechnology,2024:16:1918.
18. Van Der Maaden K, Jiskoot W, Bouwstra J. Microneedle technologies for (trans) dermal drug and vaccine delivery. Journal of Controlled Release,2012:161:645–655.
19. Bala P, Jathar S, Kale S, Pal K. Transdermal drug delivery system (TDDS), A multifaceted approach for drug delivery. Journal of Pharmacy Research,2014:8(12):1805–1835. https://www.semanticscholar.org/paper/Transdermal-Drug-Delivery-System-(TDDS)-A-Approach-Bala-Jathar/3d97b69ca9cb7dcea5d9d5b46fefa3842e8bd84
20. Alvi IA, Madan J, Kaushik D, Sardana S, Pandey RS, Ali A. Comparative study of transfersomes, liposomes, and niosomes for topical delivery of 5-fluorouracil to skin cancer cells, Preparation, characterization, in-vitro release, and cytotoxicity analysis. Anti-Cancer Drugs,2011:22:774–782.
21. Parhi R, Mandru A. Enhancement of skin permeability with thermal ablation techniques, Concept to commercial products. Drug Delivery and Translational Research,2021:11:817–841.
22. Bouwstra JA. The skin, a well organize membrane. Colloids and Surfaces, A, Physicochemical and Engineering Aspects,1997:123:403–413.
23. 10-chik z. Pharmacokinetic studies for the development of transdermal drug delivery systems, doctoral dissertation.
24. Zhang k, aslan ab. Ai technologies for education, recent research & future directions. Computers and Education, Artificial Intelligence,2021:2:100025.
25. Harrer S, Shah P, Antony B, Hu J. Artificial intelligence for clinical trial design. Trends in Pharmacological Sciences,2019:40(8):577–591.
26. Bleicher LS, van Daelen T, Honeycutt JD, Hassan M, Chandrasekhar J, Shirley W, Tsui V, Schmitz U. Enhanced utility of AI/ML methods during lead optimization by inclusion of 3D ligand information. Frontiers in Drug Discovery,2022:2:1074797.
27. Albayati N, Talluri SR, Dholaria N, Michniak-Kohn B. AI-Driven Innovation in Skin Kinetics for Transdermal Drug Delivery, Overcoming Barriers and Enhancing Precision. Pharmaceutics,2025:17(2):188.

28. Goswami DS, Uppal N, Goyal S, Mehta N, Gupta AK. Permeation enhancer for TDDS from natural and synthetic sources, A review. Journal of Biomedical and Pharmaceutical Research,2013:2:19–29.
29. Abdallah RM, Hasan HE, Hammad A. Predictive modeling of skin permeability for molecules, Investigating FDA-approved Drug permeability with various AI algorithms. PLOS Digital Health,2024:3:e0000483.
30. Defraeye T, Bahrami F, Rossi RM. Inverse mechanistic modeling of transdermal drug delivery for fast identification of optimal Model parameters. Frontiers in Pharmacology,2021:12:641111.
31. Bajwa MN, Muta K, Malik MI, Siddiqui SA, Braun SA, Homey B, Dengel A, Ahmed S. Computer-aided diagnosis of skin diseases using deep neural networks. Applied Sciences,2020:10:2488. Doi: 10.3390/app10072488.
32. Joshi N, Machekposhti SA, Narayan RJ. Evolution of transdermal drug delivery devices and novel microneedle technologies, A historical perspective and review. JID Innovations,2023:3:100225. Doi: 10.1016/j.xjidi.2023.100225.
33. Alshehri S, Hussain A, Altamimi MA, Ramzan M. In vitro, ex vivo, and in vivo studies of binary ethosomes for transdermal delivery of acyclovir, A comparative assessment. Journal of Drug Delivery Science and Technology,2021:62:102390.
34. Kaur A, Sharma G, Gupta V, Ratho RK, Shishu, Katare OP. Enhanced acyclovir delivery using w/o type microemulsion, Preclinical assessment of antiviral activity using murine model of zosteriform cutaneous HSV-1 infection. Artificial Cells, Nanomedicine, and Biotechnology,2018:46:346–354. Doi: 10.1080/21691401.2017.1313262.
35. Kang G, Kim M, Lee Y, Yang H, Seong B-L, Jung H. Egg microneedles for transdermal vaccination of inactivated influenza virus. Biomaterials Science,2024:12:907–918. Doi: 10.1039/D3BM01635H.
36. Gupta P, Özel B, Stanczyk FZ, Felix JC, Mishell Jr DR. The effect of transdermal and vaginal estrogen therapy on markers of postmenopausal estrogen status. Menopause,2008:15:94–97. Doi: 10.1097/gme.0b013e318148b98b.
37. He W, Kong S, Lin R, Xie Y, Zheng S, Yin Z, Huang X, Su L, Zhang X. Machine Learning Assists in the Design and Application of Microneedles. Biomimetics,2024:9:469. Doi: 10.3390/biomimetics9080469.
38. Xu C, Wu Y, Zhao L, Zhou W, Li Y, Yi X, Wang Y, Zhang Q, Hu H, Wang Z. Transdermal hormone delivery, Strategies, application and modality selection. Journal of Drug Delivery Science and Technology,2023:86:104730.
39. Files J, Kling JM. Transdermal delivery of bioidentical estrogen in menopausal hormone therapy, A clinical review. Expert Opinion on Drug Delivery,2020:17:543–549. Doi: 10.1080/17425247.2020.1700949.
40. Ahad A, Aqil M, Kohli K, Sultana Y, Mujeeb M, Ali A. Interactions between novel terpenes and main components of rat and human skin, Mechanistic view for transdermal delivery of propranolol hydrochloride. Current Drug Delivery,2011:8:213–224.
41. Onesti G, Bock KD, Heimsoth V, Kim KE, Merguet P. Clonidine, A new antihypertensive agent. American Journal of Cardiology,1971:28:74–83.
42. Nicholls M. Nitric oxide discovery Nobel Prize winners, Robert, F, Furchgott, Louis, J. Ignarro, and Ferid Murad shared the Noble Prize in 1998 for their discoveries concerning nitric oxide as a signalling molecule in the cardiovascular system. European Heart Journal,2019:40:1747–1749.
43. Onesti G, Bock KD, Heimsoth V, Kim KE, Merguet P. Clonidine, A new antihypertensive agent. American Journal of Cardiology,1971:28:74–83.
44. Kennedy GM, Lhatoo SD. CNS adverse events associated with antiepileptic drugs. CNS Drugs,2008:22:739–760.
45. Winblad B, Cummings J, Andreasen N, Grossberg G, Onofrj M, Sadowsky C, Zechner S, Nagel J, Lane R. A six-month double-blind, randomized, placebo-controlled study of a transdermal patch in Alzheimer's disease, rivastigmine patch versus capsule. International Journal of Geriatric Psychiatry,2007:22:456–467.
46. Amsterdam JD. A double-blind, placebo-controlled trial of the safety and efficacy of selegiline transdermal system without dietary restrictions in patients with major depressive disorder. Journal of Clinical Psychiatry,2003:64:208–214.
47. Ramesh G, Vamshi Vishnu Y, Kishan V, Madhusudan Rao Y. Development of nitrendipine transdermal patches, in vitro and ex vivo characterization. Current Drug Delivery,2007:4:69–76.
48. Levin G, Kornfeld J, Patel Y R, Damon S. Transdermal Delivery, Success Through a Deep Understanding of The Skin. Corium. [Serial Online]. 2007 [cited 2011 Oct 08]. Available online, URL: http://www.ondrugdelivery.com.
49. Joseph S D. Transdermal Patches, An Innovative Drug Delivery System That Has Raised Serious Safety Concerns. NewsInferno. [Serial online]. 2006 [cited 2011 Feb 22]. Available online, URL: http://www.newsinferno.com.
50. Morrow T. Transdermal Patches Are More Than Skin Deep. Managed Care. [Serial online]. 2004 [cited 2011 Feb 4]. Available online, URL: http://www.managedcaremag.com.
51. Shah S. Transdermal Drug Delivery Technology Revisited, Recent Advances. Pharmainfo.net,2008:6(5).
52. Wang FY, Chen Y, Huang YY, Cheng CM. Transdermal drug delivery systems for fighting common viral infectious diseases. Drug Delivery and Translational Research,2021:11:1498–1508. https://doi.org/10.1007/s13346-021-01004-6
53. Rizvi SMD, Hussain T, Alshammari F, Sonbol H, Ahmad N, Faiyaz SSM, Kamal MA, Khafagy ES, Moin A, Abu Lila AS. Nano-conversion of ineffective cephalosporins into potent one against resistant clinical uro-pathogens via gold nanoparticles. Nanomaterials,2023:13:475. https://doi.org/10.3390/nano13030475
54. Abdallah RM, Hasan HE, Hammad A. Predictive modeling of skin permeability for molecules, Investigating FDA-approved drug permeability with

various AI algorithms. PLOS Digital Health,2024:3:0000483.
55. Serrano DR, Luciano FC, Anaya BJ, Ongoren B, Kara A, Molina G, Ramirez BI, Sánchez-Guirales SA, Simon JA.
56. Tomietto G. Artificial intelligence (AI) applications in drug discovery and drug delivery, Revolutionizing personalized medicine. Pharmaceutics,2024:16:1328.