GLOBAL JOURNAL OF PHARMACEUTICAL AND SCIENTIFIC RESEARCH
(GJPSR)

Volume-1, Issue-1, August- 2025

Article Received on 03/07/2025 Article Revised on 22/07/2025 Article Accepted on 11/08/2025

ARTIFICIAL INTELLIGENCE IN TOPICAL DOSAGE FORM DEVELOPMENT

[1] Pallavi Tiwari, [2]Vimal K Yadav, [2]Vishnu Prasad Yadav, [2]Vineet Bharti, [2]Kunal Agam, [3]Maya Sharma, [4]Rahul Maurya

[1]Department of Chemistry, KAPG College, Prayagraj, U.P - 211002 India.

[2]Institute of Pharmacy, Dr. Rammanohar Lohia Avadh University, Ayodhya, Uttar Pradesh, India

[3] Pacific College of Pharmacy, Pacific Higher Education and Research University Udaipur, Rajasthan 313003, India.

[4]National Ayurveda Research Institute for Panchakarma, Cheruthuruthy, Thrissur, Kerala, 67953, India

Corresponding Author: Pallavi Tiwari

Abstract:

In pharmaceutical research and development, artificial intelligence (AI) has become a game-changing tool that provides creative answers to problems with dosage form optimization and drug formulation. The application of AI approaches to topical dosage form development is examined in this work, with a particular emphasis on formulations intended for transdermal, ophthalmic, and dermatological delivery systems. By utilizing artificial intelligence (AI) algorithms like machine learning, deep learning, and computer modeling, scientists can accelerate the drug formulation process, improve treatment efficacy, and reduce side effects. The application of artificial intelligence (AI) has made it possible to anticipate physicochemical qualities, identify the best excipients, and optimize formulations to meet patient needs and specific therapeutic targets. AI also helps in the development of innovative drug delivery methods with enhanced bioavailability and regulated release profiles, such as hydrogels and nanocarriers. Notwithstanding noteworthy progress, certain obstacles still exist, such as the requirement for extensive data sets, the verification of models produced by AI, and regulatory concerns. Future application of AI technology could transform the creation of topical dosage forms, resulting in formulations that are safer, more effective, and more patient-centered.

Keywords: Artificial Intelligence, topical dosage form development, machine learning, deep learning, and computational modelling.

1. Introduction

The pharmaceutical sector is dealing with an increasing array of difficulties, such as rising expenses, rising complexity, and rising regulatory demands. AI has the ability to dramatically increase drug development's effectiveness, precision, and speed while also improving patient outcomes. Enhanced efficiency is among the pharmaceutical industry's main advantages of artificial intelligence. Large volumes of data from many sources can be analyzed by AI an algorithm, which cuts down on the time and expense involved in medication development. By determining which patients will respond best to a given medication and forecasting their response, it can also be used to expedite clinical studies and cut down on their cost and duration. Increased precision in the pharmaceutical sector is one of AI's main advantages.

Artificial intelligence (AI) algorithms can be used to evaluate data from many sources in order to find novel drug targets, forecast toxicity, and increase prediction accuracy. Researchers can make better decisions on the creation of novel medicines by using AI to assess data from many sources. This lowers the likelihood of failure and raises the success rate of drug development overall. And last, AI may help patients receive better care. Personalized treatment plans based on a patient's genetic and medical data can be created using AI algorithms, increasing treatment efficacy and lowering the chance of unfavorable outcomes. Artificial intelligence (AI) can also be used to track real-world data in order to spot adverse events and enhance medication safety, guaranteeing that patients receive effective and safe care. In summary, artificial intelligence (AI) holds great promise for enhancing the pharmaceutical industry's patient outcomes and drug development process's speed, accuracy, and efficiency. Artificial Intelligence (AI) has the potential to improve medication safety, expedite clinical trials, create customized therapies, and evaluate data from many sources. Artificial intelligence (AI) has the potential to expedite the time to market for innovative treatments while simultaneously raising the standard of healthcare (Yang et al., 2019).

2. Background of Topical Dosage Forms:

Topical dosage forms are pharmaceutical formulations intended for application to the skin or mucosal surfaces to exert local or, in some cases, systemic effects. These include ointments, creams, gels, lotions, pastes, foams, and transdermal patches. The historical use of topical agents dates back to ancient civilizations, where natural products like herbal pastes and oils

were used for treating wounds and skin ailments (Pathan & Setty, 2009). In modern pharmaceutical science, topical formulations are widely used for treating dermatological conditions such as psoriasis, acne, eczema, and localized infections due to their ability to deliver the drug directly to the site of action, thereby minimizing systemic exposure and side effects (Prausnitz & Langer, 2008). The skin, although a strong protective barrier, is a viable route for drug delivery, particularly when enhanced by formulation techniques that improve penetration. Key considerations in developing topical dosage forms include drug solubility, partition coefficient, molecular weight, formulation base, and skin condition (Barry, 2001). Recent advancements such as nanoemulsions, liposomes, ethosomes, and transferosomes have been explored to overcome the limitations of skin permeability and enhance drug absorption and bioavailability (Honeywell-Nguyen & Bouwstra, 2005). These innovations continue to support the growing significance of topical drug delivery systems in both therapeutic and cosmetic applications.

Table 1: Types of Topical Dosage Forms and Their Key Characteristics

Dosage Form	Base Type	Appearance	Key Characteristics	Common Uses
Ointment	Oleaginous	Greasy, semi-solid	Occlusive, long retention, good for dry skin	Psoriasis, eczema, burns
Cream	Emulsion (O/W or W/O)	Semi-solid, smooth	Non-greasy (O/W), moisturizing, easy to spread	Dermatitis, fungal infections
Gel	Aqueous or hydroalcoholic	Transparent or translucent	Non-greasy, cooling effect, good for hairy areas	Acne, inflammation, muscle pain
Lotion	Liquid emulsion	Fluid, thin	Easy to apply on large or hairy areas, non-greasy	Sunburn, itching, mild irritation
Paste	High solid content	Thick, stiff	Protective, stays on skin longer, absorbs secretions	Diaper rash, ulcers
Foam	Pressurized	Light, airy	Spreads easily, good	Scalp conditions,

	(aerosol)		penetration, cosmetically acceptable	corticosteroids
Transdermal Patch	Polymer-based film	Discrete patch	Controlled, systemic drug delivery, avoids first-pass metabolism	Pain management, hormone therapy

3. Emergence of Artificial Intelligence in Pharmaceutical Sciences:

The emergence of artificial intelligence (AI) has significantly transformed pharmaceutical sciences, offering innovative solutions in drug discovery, development, and personalized medicine. AI algorithms, including machine learning (ML), deep learning (DL), and natural language processing (NLP), are being widely applied to accelerate the identification of drug targets, optimize molecular structures, and predict pharmacokinetic and pharmacodynamic profiles (Mak & Pichika, 2019). These tools enhance the accuracy and efficiency of processes such as virtual screening, de novo drug design, and structure–activity relationship modeling. In clinical development, AI supports patient recruitment, trial design, and real-time data monitoring, thereby reducing time and cost (Topol, 2019). Furthermore, AI contributes to formulation science by optimizing excipient combinations and predicting stability profiles, while also playing a pivotal role in pharmacovigilance through the automated detection of adverse drug reactions from large datasets (Shameer et al., 2018). The integration of AI with big data, genomics, and computational chemistry has opened avenues for personalized and precision medicine, ensuring tailored therapies based on individual genetic profiles. As AI continues to evolve, its ethical implementation and regulatory adaptation are essential to fully realize its potential in reshaping pharmaceutical research and healthcare delivery.

Table 2: Comparison of traditional vs AI-based drug development

Parameter	Traditional Drug Development	AI-Based Drug Development
Time Consumption	10–15 years on average	Significantly reduced (can cut several years)
Cost	$2–3 billion on average	Lower cost due to optimized processes
Target Identification	Relies on lab experiments and known pathways	Uses big data and algorithms to identify novel targets

Hit/Lead Identification	Manual screening and in vitro assays	Virtual screening using machine learning & deep learning
Preclinical Testing	Empirical animal studies and manual analysis	Predictive modeling to refine compound selection
Clinical Trial Design	Standard protocol with limited personalization	Adaptive trial designs, patient stratification using AI
Adverse Event Detection	Based on reported side effects during trials and post-marketing	Real-time monitoring using EHRs and pharmacovigilance databases
Data Handling	Manual or semi-automated data analysis	Automated high-throughput analysis of complex datasets
Success Rate	Low success rate due to high attrition	Improved probability through predictive analytics
Personalization	Limited personalization	Personalized drug development based on genomics and patient data
Decision-Making	Experience-driven, slower	Data-driven, faster, with continuous feedback integration

4. Applications of AI in Pharmaceutical Industry:

Numerous AI applications exist in the healthcare and pharmaceutical sectors, with the potential to revolutionize important elements of the sector and spur innovation. We'll talk about a few of the most significant uses of AI below.

(a) Drug Discovery:

The act of finding new drugs to market, developing and testing novel chemical entities, and identifying possible therapeutic targets are all part of the difficult and time-consuming process of drug development. Artificial intelligence (AI) has the ability to completely transform the drug discovery process by evaluating enormous volumes of data from several sources, finding novel therapeutic targets, and forecasting probable toxicity and side effects. The conventional drug discovery process is a data-intensive approach that primarily uses a variety of computational and experimental techniques to forecast toxicity and find novel targets. AI algorithms can analyze vast volumes of data from many sources, such as chemical databases, scientific literature, and genetic and proteomic data, to lessen these laborious activities. AI can discover novel targets, anticipate toxicity, rank chemicals for additional research, and steer clear of substances that are probably harmful by merging data from

several sources. In order to find viable treatment targets for a variety of illnesses, such as cancer, cardiovascular disease, and neurological disorders, AI algorithms can be used to evaluate genomic and proteomic data. AI is useful, for instance, in the analysis of gene expression data to pinpoint targets for cancer treatments or in the analysis of protein-protein interaction data to pinpoint targets for neurological disorders. Toxicology prediction is one of the key uses of AI in drug discovery. AI algorithms can be used, for instance, to forecast a compound's propensity to produce liver toxicity or its likelihood of producing cardiovascular toxicity (Paul et al., 2021, Patil et al., 2021).

(b) Clinical Trial and Designs:

Clinical trials are vital for evaluating the safety and efficacy of new treatments but are often expensive and time-consuming. Artificial intelligence (AI) can streamline this process by improving efficiency and reducing costs. One key application is patient selection, where AI analyzes genetic, medical, and demographic data to identify individuals most likely to respond to treatment, reducing trial size and duration (Akhondzadeh et al., 2016). AI also predicts patient responses, helping optimize dosages and treatment plans. Additionally, AI can monitor adverse events by detecting side effects early, enhancing trial safety (Zhong et al., 2018). Furthermore, AI enables real-time data analysis and adaptive trial designs, allowing researchers to make quicker adjustments and improve decision-making. This integration of AI can significantly accelerate drug development while maintaining accuracy and patient safety.

(c) Personalized Medicine:

The goal of personalized medicine, a new area in healthcare, is to use a patient's genetic and medical data to customize a treatment plan to meet their specific needs. By empowering medical professionals to create customized treatment regimens that are tailored to each patient, personalized medicine holds the potential to completely transform the way diseases are managed. With its capacity to evaluate enormous volumes of genomic and medical data in order to find novel therapeutic targets and forecast treatment response, artificial intelligence (AI) is becoming more and more significant in the field of personalized medicine. Researchers can create novel treatments that are tailored to the needs of individual patients by using AI algorithms to find patterns in patient data that are connected to certain diseases or ailments. The creation of predictive models is one of the main uses of AI in personalized medicine. Artificial intelligence (AI) systems can evaluate patient data and forecast how a patient will react to a specific treatment. With the use of this data, customized

medications that are tailored to each patient's specific genetic and medical profile can be created. The identification of novel

therapeutic targets is a significant application of artificial intelligence in personalized medicine. Genomic and medical data can be analyzed by AI systems to find new drug development targets. By using AI to find new therapeutic targets, scientists can create new medications tailored to each patient, increasing the efficacy of the treatment as a whole (Awwalu et al., 2015).

Table 3: Commonly Used AI and Machine Learning Algorithms in Pharmaceutical Research

Algorithm	Type	Application in Pharma	Key Features
Random Forest	Supervised Learning	ADMET prediction, feature selection, toxicity analysis	High accuracy, handles large data sets
Support Vector Machine	Supervised Learning	Drug-target interaction, classification of bioactivity	Effective for high-dimensional data
k-Nearest Neighbors (k-NN)	Supervised Learning	Drug classification, similarity analysis	Simple, intuitive, good for pattern recognition
Neural Networks (NN)	Deep Learning	Molecular property prediction, de novo drug design	Captures complex nonlinear relationships
Convolutional Neural Networks (CNN)	Deep Learning	Image analysis in histopathology, molecular imaging	Spatial pattern recognition
Recurrent Neural Networks (RNN)	Deep Learning	Sequence-based tasks, such as protein folding and genomics	Good for temporal and sequential data
Principal Component Analysis (PCA)	Unsupervised Learning	Dimensionality reduction, data visualization	Simplifies data, helps identify key variables
k-Means Clustering	Unsupervised Learning	Drug repurposing, patient subgroup identification	Groups similar data points, unsupervised

Natural Language Processing (NLP)	AI Technique	Literature mining, pharmacovigilance, clinical documentation analysis	Understands and processes human language

5. Analyzing Data for New Drug Development:

Artificial Intelligence (AI) holds promise for optimizing the drug development process through enhanced productivity and cost reduction. As a result, analyzing data from many sources is one of the main uses of AI in drug development. Artificial intelligence (AI) algorithms can be used to evaluate data from many sources, including preclinical research, clinical trials, and electronic health records, in order to find new drug targets and forecast how well patients will respond to various therapies. AI can be used in these circumstances to examine data from many sources. Additionally, by using better information, researchers can shorten the time and lower the expense of the drug discovery process while also developing novel medicines. The optimization of preclinical research is a significant use of AI in drug development. Preclinical data can be analyzed by AI algorithms to determine which candidates are most promising for additional research and development. When it comes to optimizing medicines during preclinical investigations, AI is far more effective and valuable. Researchers can shorten the time and lower the cost of the drug development process by using AI to limit the number of prospective NCEs that are chosen for additional development (Lee et al., 2022).

6. Enhancing Drug Safety:

One of the most important aspects of medication research is making sure the drugs are safe. Through the monitoring and analysis of real-world data, artificial intelligence (AI) has the potential to improve drug safety by identifying adverse events. AI can be used to analyze data from a variety of sources, including electronic health records, claims data, and patient-generated data, to identify adverse events that might not have been discovered during clinical trials. This is because one of the main uses of AI in drug safety is the analysis of real-world data. By using AI to examine real-world data, scientists can find new safety issues and enhance the general safety of medications that have previously received approval. Monitoring adverse occurrences is a crucial use of AI in medication safety. Artificial intelligence (AI) systems can monitor real-world data to spot negative events and follow their evolution over time. New tactics for lowering the possibility of side effects and enhancing medication safety can be created using this information. Therefore, by tracking and evaluating real-world data

to identify adverse occurrences and develop medication safety, AI is a very promising approach to play a crucial role in boosting drug safety and ultimately improve the quality of healthcare provided (Basile et al., 2019).

7. Impact of AI and Tools on Pharmaceutical Industry:

The pharmaceutical business is impacted by a number of AI tools and methodologies, particularly those related to drug development and discovery. These are explained in the sections that follow.

(a) Machine learning (ML) algorithms: In the pharmaceutical sector, machine learning (ML) methods like support vector machines, decision trees, and random forests are frequently used to evaluate vast volumes of data in order to forecast toxicity, find new drug targets, and increase prediction accuracy.

(b) Natural language processing: In order to gain insights and enhance decision-making in the pharmaceutical industry, natural language processing (NLP) algorithms are utilized to evaluate unstructured data, such as electronic health records and scientific literature.

(c) Deep learning algorithms: Convolution neural networks and recurrent neural networks are two examples of deep learning algorithms (DLA) that are used to evaluate complicated data sets, like genetic and imaging data, in order to create individualized treatment regimens and increase prediction accuracy.

(d) Predictive analytics algorithms: Clinical trials and electronic health records are two examples of the data sets that predictive analytics algorithms (PLA) are used to examine in order to forecast patient outcomes increase the effectiveness of clinical trials, and find novel therapeutic targets.

(e) Robotics process automation: RPA, or robotic process automation, is a tool used to streamline the drug development process by automating repetitive processes. These are some of the AI methods and resources that the pharmaceutical industry uses most frequently, and they have the power to have a big influence on every facet of drug development and discovery.

8. Impact of AI and Tools on Topical Delivery Systems

8.1 In Silico Assessment of Oral and Percutaneous Administration

Recent years have seen substantial changes in the pharmaceutical sector, mostly brought about by the need to expedite medication discovery, competitive market conditions, and

regulatory standards. Model-informed drug development (MIDD) is a technique that uses quantitative computing models to speed up decision-making. This method clarifies the intricate relationship between how well a medicine works and the clinical results that follow. The goal of this thorough analysis is to clarify the processes that govern how medications dissolve, release, and then pass through biological membranes. It also highlights how crucial it is to simulate these processes using a range of in silico models. An analytical framework for comprehending the kinetics of transit, dissolution, and absorption related to oral medication administration is offered by sophisticated compartmental absorption models. On the other hand, molecular dynamics simulations and quantitative structure-penetration interactions are primarily used to estimate drug permeation in topical and transdermal drug delivery systems. This overview discusses a range of modeling approaches, from empirical equations to mechanistic models, and emphasizes the increasing significance of cutting-edge technologies like artificial intelligence, sophisticated imaging, and spectroscopic methods (Djuris et al., 2024).

Table 4: Impact of AI Tools on Topical Delivery Systems

Application Area	AI Integration	Benefits
In Silico Modeling for Drug Absorption	AI with molecular dynamics and QSPR models	Simulates dissolution, release, and membrane permeation processes accurately
Adhesion Prediction for Transdermal Systems	Deep learning models using mobile image capture and AI	Reduces observer bias, enables real-world performance prediction (Wang et al., 2023)
Solvent Impact on Skin Permeability	SVR and RF models trained on curated datasets	Accurately predicts solvent effects on permeability without physical trials (Baba et al., 2015)

9. Artificial Intelligence to Improve the Calculation of Percent Adhesion for Transdermal Delivery Systems

When it comes to transdermal and topical delivery systems (TDS), adhesion is an essential component of quality and performance. To support the approval of TDS in both new drug

applications and abbreviated new drug applications, regulatory agencies advise conducting in vivo skin adhesion tests. Currently, the method of assessment used in these types of studies relies on visual observation of the percent adhesion, which is the ratio of the total TDS area to the area of TDS connected to the skin. Variability and bias are introduced by visually judged % adherence by trial participants or qualified physicians. Furthermore, trial subjects are usually housed in clinical centers for the duration of the product wear period, which could cause problems when extrapolating adhesion performance to real-world situations. In this study, we propose to assist and automate the process of gathering photographic evidence and estimating the % adherence by utilizing mobile technologies and artificial intelligence. We utilized cutting-edge methodologies and internally curated data to train cutting-edge deep learning models. The trained models perform well, according to the results, and further research is being done on the models' possible application in clinical settings (Wang et al., 2023).

10. ML-Based Optimization of Gel and Cream Formulations

The optimization of gel and cream formulations has traditionally relied on trial-and-error approaches, which are time-consuming and resource-intensive. The integration of machine learning (ML) into pharmaceutical formulation offers a transformative solution by enabling data-driven prediction and optimization of formulation parameters. ML algorithms such as support vector machines, random forests, and artificial neural networks have demonstrated considerable success in predicting key formulation attributes, including viscosity, spreadability, drug release profiles, and stability under varying conditions (Gupta et al., 2020). For instance, artificial neural networks have been applied to model the influence of different polymer and surfactant concentrations on the rheological behavior and drug diffusion rates in topical gels (Patel et al., 2021). Similarly, ML-based design of experiments (DoE) can reduce experimental runs while improving formulation accuracy, helping to identify the optimal composition more efficiently (Alsulays et al., 2022). These techniques not only accelerate the development timeline but also enhance the reproducibility and performance of the final product, making ML an indispensable tool in modern formulation science.

11. Prediction of Solvent Effect on Human Skin Permeability

For the purpose of evaluating the efficacy and toxicological risk of novel dermatological formulations in the development of pharmaceuticals and cosmetics, the influence of solvents on skin permeability is significant. Effective and trustworthy prediction models could provide

light on the various mechanisms underlying the solvent effect. However, low predictive accuracy and a limited diversity of permeants and mixture components archived in databases have hindered such prediction models. Here, we offer a resolution to both issues.

First, we assembled a fresh huge database comprising 412 samples from 31 solvents and 261 structurally different permeants that have been documented in the literature. The data were meticulously vetted to guarantee that they were collected under regular experimental settings. We then used random forest (RF) with greedy stepwise descriptor selection in conjunction with support vector regression (SVR) to build a high-performance predictive model using our datasets. The models underwent both internal and external validation.

Comparing performance statistics, the SVR outperformed the RF. 0.899, 0.351, and 0.268, respectively, were the (externally confirmed) determination coefficient, root mean square error, and mean absolute error of SVR. Furthermore, our approach can predict as-yet-unsynthesised molecules because all descriptors are entirely computational.For assessing potential pharmaceutical and cosmetic candidates and refining skin-permeable topical formulations, our high-performance prediction model presents a compelling substitute to permeability studies (Baba et al., 2015).

12. Assessment of diffusion coefficient from mucoadhesive barrier devices

In a female controlled drug delivery system (FcDDS), the objective of this study is to clarify the physicodynamic phenomena driving the diffusion coefficient (D) of the loaded pharmaceuticals and to identify the most influential variable on the diffusivity using artificial neural networks (ANN). Using an in vitro device called the Simulant Vaginal System (SVS), release profiles of sodium dodecyl sulphate (SDS), a topical microbicide utilized as a model medication, were acquired from FcDDS under different settings. Artificial neural networks were used to evaluate the effects of formulation and intrinsic/extrinsic variables on the diffusivity of SDS (ANN). The diffusivity and formulation/physiological factors showed a non-linear connection, as demonstrated by the release patterns of SDS from FcDDS. When determining the diffusion coefficient of SDS from FcDDS, intrinsic variables (vaginal fluid pH and secretion rate) are more important than formulation variables (formulation loading weight and loaded dosages in the formulation) or extrinsic variables (inserting position). The vaginal fluid pH is the most important variable (out of five) in determining the maximum value of 0.95+/-0.04 for the diffusion coefficient of SDS from FcDDS. The effects of the formulation variables on the SDS diffusion coefficient were manifestly overshadowed by the external exposure circumstances. Under the specified circumstances, a model-based method

can be utilized to evaluate the diffusion coefficient of loaded medications in FcDDS, providing a highly confident parameter-specific STD prevention strategy (Lee et al., 2008).

13. Soft robotic devices for site-specific drug delivery

The development of different drug delivery systems (DDS), including chemical, biological/molecular, and mechanical/physical DDS, has received a lot of attention lately. The goal of site-specific drug delivery, which is based on mechanical/physical systems that include implantable and robotic drug delivery systems, is to transport a drug or therapeutic agent to a desired location within the body and release it as desired with comparatively small toxicity and side effects compared to classical drug administration means like peroral, parenteral, transmucosal, topical, and inhalation. The terms site-specific, controlled, targeted, and smart drug delivery are used interchangeably in the literature. We cover implanted DDS, which are more advanced than robotic DDS, in order to highlight design and performance requirements, look into problems related to robotic DDS, and emphasize the robotic or autonomous DDS, which can be reprogrammed and deliver multiple doses of a drug at a required time and rate. In order to outline the research obstacles we must overcome in order to develop soft robotic devices for clinical and biomedical applications, critical research topics pertaining to both DDSs are provided (Alici et al., 2015).

14. Production of lipid nanoparticles for skin cancer treatment

The goal of this project is to combine the benefits of lipid nanoparticles with the Quality by Design (QbD) methodology to create a novel medication delivery system that can treat aktinic keratosis and skin cancer. Because lipid nanoparticles can penetrate the skin more deeply and get past the intricate structure of the skin barrier, they are among the most effective choices for the topical treatment of skin problems. All of the product's variables should be explained because the formulation creation process involves complicated variables involving active substances, raw materials, or production techniques. In order to accomplish a time- and money-saving procedure guaranteeing a high-quality product, the QbD approach—which refers to design and develop formulations and manufacturing processes to preserve the mandated product quality—was also effectively employed. Following QbD procedures, solid lipid nanoparticles and nanostructured lipid carriers loaded with 5-fluorouracil (5-FU) were created and characterized. Artificial Neural Networks have been used to achieve optimal lipid nanoparticle formation with guaranteed quality that was within the design space. The high pressure homogenization approach created the ideal lipid nanoparticle formulation, which is

an NLC formulation with a mean particle size of 205,8 ± 9,34 nm, narrow size distribution (0.279 ± 0.01), and negative zeta potantial -30,20 ± 0,92.

Human keratinocyte and epidermoid cancer cell culture investigations were used to establish the cytotoxicity profiles of the ideal NLC. Compared to free 5-FU, optimal NLC exhibited a much greater anticancer impact on epidermoid carcinoma cells and less cytotoxicity on human keratinocyte cells. For simplicity of application, optimal NLC was developed in a hydrogel formulation with the right viscocity, pH, occlusive and mechanical qualities, and patient compliance. Following the application of NLC enriched hydrogel and 5-FU hydrogel, respectively, the cumulative amount of 5-FU in the dermal tissues of rat skin was found to be 20.11 ± 2.14 µg/cm2 and 9.73 ± 0.87 µg/cm2. In conclusion, this study shown that QbD guided formulation development study with artificial neural network assistance can yield a time and cost-saving procedure guaranteeing a high-quality output. It is possible to treat skin malignancies topically with a new semisolid dose form enhanced by NLC (Amasya et al., 2019).

15. Semi-Solid Dosage Forms as Topical Therapy for Local Inflammation

In an innovative move to improve the biopharmaceutical profile of pranoprofen (PRA) for dermal administration in the treatment of skin inflammation that may be brought on by a potential skin abrasion, pranoprofen (PRA)-loaded nanostructured lipid carriers (NLC) have been dispersed into blank gels made of 1% of Carbomer 940 (PRA-NLC-Car) and 3% of Sepigel® 305 (PRA-NLC-Sep). The goal of this strategy is to strengthen PRA's adhesion to the skin, enhancing its retention and anti-inflammatory properties. A number of characteristics, including pH, morphology, rheology, and swelling, were assessed for gels. Franz diffusion cells were used for ex vivo skin penetration and in vitro drug release studies. Furthermore, human tolerance studies were conducted by assessing the biomechanical features, and in vivo experiments were conducted to assess the anti-inflammatory impact. The rheological profile of semi-solid pharmaceutical forms for topical application was found to be typical, with a sustained release lasting up to twenty-four hours. The effectiveness of PRA-NLC-Car and PRA-NLC-Sep in an inflammatory animal model research was confirmed histologically by in vivo experiments conducted on Mus musculus mice and hairless rats. The gels were well accepted, and there were no indications of skin irritation or changes in the biophysical characteristics of the skin. The investigation's findings showed that the semi-solid formulations that were created fit the bill as a drug delivery vehicle for PRA's transdermal delivery, improving its dermal retention and indicating that they might be used as an

intriguing and successful topical treatment for localized skin inflammation brought on by a potential abrasion (Ahmadi et al., 2023).

16. Expert Systems for Predicting the Bioavailability in Cosmetic Products

A cosmetic formulation's ability to passively traverse the stratum corneum and permeate into the skin layers is restricted to a small number of molecules. However, because of the possibility of adverse consequences, some active ingredients—like sunscreens—should never come into contact with the skin in high quantities. In light of the growing importance of artificial intelligence as a prediction tool, we have chosen the Formulating for Efficacy® Software to predict changes in the bioavailability of specific topical cosmetic chemicals. Different oils were identified as having poor release capability using the Franz diffusion cell methods, and these were compared to the oils recommended by the program in formulations containing benzophenone-3. The lipophilic phases, if included in the emulsion, were predicted by the software to be stable and occasionally even more palatable in consistency and appearance than the formulator's reference emulsions. However, Formulating for Efficacy® Software is still limited in its ability to anticipate the hydrophilic phase and does not allow the user to select the preservative system or emulsifier (Baldisserotto et al., 2022).

17. Microrobots: a new era in ocular drug delivery

Treatments for a number of conditions affecting the anterior and posterior regions of the eye may be altered by ocular microrobots. An avenue for minimally invasive targeted therapy is the wireless manipulation and placement of drug delivery magnetic millimeter and submillimeter platforms within the eye. Still in its infancy, the discipline faces difficulties with manufacture, control, and interaction with intricate biological ecosystems.

The intricate anatomy and physiology of the eye, which places restrictions on the existing treatments for ocular illnesses, is briefly introduced in this study. A brief discussion of the disadvantages of intravitreal injections, topical eye drops, and drug delivery implants is provided. The authors also discuss the latest developments in the creation, management, manipulation, and distribution of drugs and examine the less invasive microrobotic technique as a potential substitute. Even though the area of microrobotics is relatively new, a lot of work has been done to address various issues pertaining to the minimally invasive manipulation of microdevices in the eye. As of right now, in vivo testing for systems and their biocompatibility is the status of research. It is anticipated that the broad ideas learned will soon be used for targeted treatments, particularly for diseases of the posterior eye (Fusco et al., 2014).

18. Machine learning for sustained ocular drug delivery

Treatment of several diseases, especially chronic diseases that need long-term care, can be greatly aided by sustained medication delivery techniques. The requirement for repeated intraocular injections and patient adherence to eye drop dose regimens are major obstacles to efficient disease management for many chronic ocular illnesses. Here, we use peptide engineering to give peptide-drug conjugates the ability to bind to melanin, enabling them to function as a sustained-release depot in the eye. With the aid of super learning-based technology, we synthesize multifunctional peptides that bind to melanin, efficiently penetrate cells, and show minimal cytotoxicity. For up to eighteen days following a single intracameral injection in rabbits, intraocular pressure decrease is seen when the lead multifunctional peptide (HR97) is conjugated to brimonidine, an intraocular pressure reducing medication prescribed for topical dosage three times daily. Furthermore, when compared to a free brimonidine injection, the cumulative intraocular pressure-lowering impact increases by almost 17 times. Multifunctional peptide-drug conjugates that have been engineered show promise in delivering long-lasting treatment in the eye and other areas (Hsueh et al., 2023).

19. Artificial neural network to optimize novel ophthalmic flexible formulations

Flexible nano-liposomes carrying pilocarpine hydrochloride (PN) (PN-FLs) were synthesized, developed, and described to enhance the topical distribution of PN to treat glaucoma. Response surface methodology (RSM) and artificial neural network (ANN) were utilized to optimize the process and produce the best possible formulation. Particle size, zeta potential, morphology, fourier transform infrared (FT-IR) spectroscopy, and entrapment efficiency (EE) of PN-FLs were among the parameters examined. According to the drug release trial, PN-FLs exhibited a significant sustained release impact. Studies from the diseased section and the modified Draize test did not suggest any possible ocular discomfort. The pre-ocular residence duration of PN, which was 1.81 times longer than that of PN solution, was considerably extended by PN-FLs, according to non-invasive fluorescence imaging. The AUC of PN-FLs in pharmacokinetic tests was 4.55 times greater than the control's. The formulations in this work were also evaluated using Molecular Dynamics (MD) modeling, a novel approach to formulation creation and improvement. All available results suggest that PN-FLs hold tremendous promise for ocular administration and could serve as a viable ocular delivery strategy for PN. Furthermore, MD simulation contributes knowledge to experimental research initiatives and is becoming more important in formulating and refining formulations (Zhao et al., 2018).

20. An Artificial Neural Network Based Analysis of Factors Controlling Particle Size

An artificial neural network (ANN) was used to construct a predictive model of a virgin coconut oil (VCO) nanoemulsion system for the topical delivery of copper peptide, an anti-aging chemical, in order to study the parameters that affect particle size. Particle size was considered the response for the trained network, whereas the amount of VCO, Tween 80: Pluronic F68 (T80:PF68), xanthan gum, and water were the four independent variables. The data were modeled using genetic algorithms (GA), which were applied to training, testing, and validation sets. The resulting model demonstrated the neural network's excellent performance as well as its capacity to pinpoint the essential components of the VCO nanoemulsion. It was discovered that xanthan gum (28.56%) was the primary factor influencing the particle size, followed by water (21.74%), T80:PF68 (26.9%), and VCO (22.8%). Particle sizes of 120.7 nm were achieved from the successful preparation of the formulation containing copper peptide under ideal conditions. The final formulation demonstrated good physical stability in the face of centrifugation, freeze-thaw cycle testing, and storage at 25°C and 45°C. It also displayed a zeta potential lower than -25 mV (Samson et al., 2016).

21. Artificial neural networks for drug release profiles from cochlear implant

One innovative way to treat post-operative issues related to cochlear implantation surgery, such as inflammation or infections, involves coating cochlear implants to release medications topically, such as corticosteroids or antibiotics. The amount and duration of medication release from these devices can be modulated by adjusting a number of variables, including formulation characteristics. Mathematical modeling of the drug release profile from a delivery device could expedite formulation and result in cost savings. A model should be able to give reliable estimates for the initial formulation parameters, such as composition, geometry, and drug loading, and vice versa, in order to achieve particular in vitro drug release characteristics. Here, dexamethasone (DEX) release profile and formulation parameters are predicted bilaterally using artificial neural networks (ANNs) from cochlear implant coatings made of porous, monolithic silicone rubber-based matrices.

The devices were made as monolithic DEX dispersions in a porogen-containing silicone rubber matrix. In order to replicate the drug release profile from the porous devices, a newly constructed mathematical function was fitted to the experimental DEX release curves, and the function coefficients were given into the network as input variables. The drug loading percentage (0.05-0.5% w/w), porogen content (5-40% w/w), and porogen type (dext or

sodium chloride particles) were the formulation variables. Additionally, the ANN was looked at to find the best formulation parameter levels to provide the desired drug release profile.

The findings shown that the most effective levels for the formulation parameters to produce a certain drug release profile and vice versa may be predicted using artificial neural networks (ANNs) to model the DEX release profile from porous cochlear implant devices.

The created artificial neural networks (ANNs) were utilized to create customized drug delivery regimes and expedite the formulation development process. Additionally, non-linear interactions between the original formulation variable(s) and the subsequent drug release patterns were successfully reproduced by ANNs (Nemati et al., 2014).

22. Challenges in Adopting AI in Pharmaceutical Industry:

The absence of precise regulatory guidance is one of the obstacles preventing AI from being widely used in the pharmaceutical sector. There are several regulatory bodies that have issued broad guidelines, but there aren't any particular rules governing the application of AI in clinical trials and drug development. This could lead to a delay in the adoption of new technologies and uncertainty for businesses creating AI-based products. Data on drug discovery is gathered from a range of sources, and inconsistent data collection practices can present serious difficulties. For instance, varying trials may measure the same parameter in disparate ways, resulting in inconsistent findings. Small and constrained drug discovery databases are common, particularly for uncommon disorders. Accurate and broadly applicable AI models may be difficult to train as a result. Inaccurate forecasts and the continuation of healthcare inequities might result from data bias. An AI model based on clinical trial data, for instance, could not be accurate for other demographic groups if the data only comprises one particular demographic group. Data noise might potentially provide problems for AI-based medication design strategies. There are many different causes of noise, such as measurement errors, outliers, and experimental errors.

According to a recent American Academy of Family Physicians (AAFP) survey, the majority of those working in the healthcare sector feel uneasy with artificial intelligence. Online polls asking 2000 national leaders about AI in healthcare were conducted in November 2018. Out of those who were interviewed, 56% stated they were uncomfortable and only 44% claimed they were at ease. When applying AI in the pharmaceutical sector, data security and privacy are critical factors to take into account, particularly when patient health data is sensitive.

Patients and healthcare professionals may find it challenging to comprehend how judgments are made and what data is being used due to the opaque nature of AI algorithms.

Strong data privacy and security policies must be put into place in order to mitigate these dangers. Adherence to regulatory frameworks like HIPAA and GDPR is crucial in order to guarantee that patient data is managed in compliance with applicable laws and regulations (Vokinger et al., 2021, Tormay et al., 2015).

23. Conclusion:

The convergence of nanotechnology, artificial intelligence, and Quality by Design (QbD) principles is revolutionizing drug delivery systems, particularly in the context of topical and ocular therapies. This chapter has explored the advanced formulation strategies for lipid nanoparticles, including Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs), which have demonstrated remarkable potential in enhancing drug penetration, retention, and controlled release for conditions such as skin cancer and local inflammation. The application of QbD, supported by artificial neural networks (ANN), ensures a systematic and efficient approach to optimize formulations while maintaining high product quality and performance.

The incorporation of 5-fluorouracil into NLCs for skin cancer treatment exemplifies how deeper dermal drug delivery and improved cytotoxicity profiles can be achieved. Similarly, semi-solid formulations like PRA-NLC-Car and PRA-NLC-Sep showcase enhanced dermal retention and anti-inflammatory effects, offering promising topical solutions for skin-related disorders. The use of ANN for predicting and optimizing particle size, drug release kinetics, and formulation parameters further underscores the capability of AI-driven systems to streamline pharmaceutical development.

In the realm of cosmetic and ocular delivery, predictive modeling tools like the Formulating for Efficacy® software and the use of microrobotics illustrate the expanding horizon of personalized and minimally invasive treatment methods. ANN and machine learning models have proven to be powerful tools for predicting bioavailability, drug distribution, and release profiles, as seen in ocular systems and cochlear implants.

However, despite these technological advancements, challenges remain. The adoption of AI in pharmaceutical formulation is hindered by regulatory ambiguity, data inconsistency, and concerns over algorithmic transparency and data security. Addressing these issues through robust frameworks and ethical guidelines will be crucial to ensure the safe and effective integration of AI technologies in healthcare.

24. Conflict of Interest

The author declares that there is no conflict of interest regarding the publication of this paper.

25. Acknowledgement

I gratefully acknowledge the contributions of all the authors whose work has been cited in this review, and whose findings have laid the foundation for this academic endeavor.

26. References:

- Alici G. Towards soft robotic devices for site-specific drug delivery. Expert Rev Med Devices. 2015;12(6):703-15. doi: 10.1586/17434440.2015.1091722. Epub 2015 Sep 28.
- Fusco S(1), Ullrich F, Pokki J, Chatzipirpiridis G, Özkale B, Sivaraman KM, Ergeneman O, Pané S, Nelson BJ. Microrobots: a new era in ocular drug delivery. Expert Opin Drug Deliv. 2014 Nov;11(11):1815-26. doi: 10.1517/17425247.2014.938633. Epub 2014 Jul 7.
- Ahmadi N(1), Rincón M(2)(3), Silva-Abreu M(1)(3), Sosa L(4), Pesantez-Narvaez J(5), Calpena AC(1)(3), Rodríguez-Lagunas MJ(6)(7), Mallandrich M(1)(3). Semi-Solid Dosage Forms Containing Pranoprofen-Loaded NLC as Topical Therapy for Local Inflammation: In Vitro, Ex Vivo and In Vivo Evaluation. Gels. 2023 May 29;9(6):448. doi: 10.3390/gels9060448.
- Amasya G(1), Aksu B(2), Badilli U(3), Onay-Besikci A(4), Tarimci N(3). QbD guided early pharmaceutical development study: Production of lipid nanoparticles by high pressure homogenization for skin cancer treatment. Int J Pharm. 2019 May 30;563:110-121. doi: 10.1016/j.ijpharm.2019.03.056. Epub 2019 Mar 29.
- Samson S(1), Basri M(1), Fard Masoumi HR(1), Abdul Malek E(1), Abedi Karjiban R(1). An Artificial Neural Network Based Analysis of Factors Controlling Particle Size in a Virgin Coconut Oil-Based Nanoemulsion System Containing Copper Peptide. PLoS One. 2016 Jul 6;11(7):e0157737. doi: 10.1371/journal.pone.0157737. eCollection 2016.
- Wang C(1), Strasinger C(2), Weng YT(2), Zhao X(2). Use of Artificial Intelligence to Improve the Calculation of Percent Adhesion for Transdermal and Topical Delivery Systems. J Med Syst. 2023 Dec 18;48(1):4. doi: 10.1007/s10916-023-02027-x.
- Hsueh HT(#)(1)(2), Chou RT(#)(3), Rai U(1)(4), Liyanage W(1)(4), Kim YC(1)(4), Appell MB(1)(5), Pejavar J(1)(2), Leo KT(1)(6), Davison C(1)(2), Kolodziejski P(1)(2), Mozzer A(1)(4), Kwon H(1)(2), Sista M(1)(7), Anders NM(8), Hemingway A(8), Rompicharla SVK(1)(4), Edwards M(4), Pitha I(1)(4), Hanes

J(1)(2)(4)(5)(6)(8), Cummings MP(9), Ensign LM(10)(11)(12)(13)(14)(15). Machine learning-driven multifunctional peptide engineering for sustained ocular drug delivery. Nat Commun. 2023 May 2;14(1):2509. doi: 10.1038/s41467-023-38056-w.

- Djuris J(1), Cvijic S(1), Djekic L(1). Model-Informed Drug Development: In Silico Assessment of Drug Bioperformance following Oral and Percutaneous Administration. Pharmaceuticals (Basel). 2024 Jan 30;17(2):177. doi: 10.3390/ph17020177.
- Baldisserotto A(1), Baldini E(1)(2), Ravarotto S(2), Cesa E(1), De Lucia D(3), Durini E(1)(2), Vertuani S(1)(2), Manfredini S(1)(2), Michniak-Kohn BB(4). Expert Systems for Predicting the Bioavailability of Sun Filters in Cosmetic Products, Software vs. Expert Formulator: The Benzophenone-3 Case. Pharmaceutics. 2022 Aug 29;14(9):1815. doi: 10.3390/pharmaceutics14091815.
- Nemati P(1), Imani M, Farahmandghavi F, Mirzadeh H, Marzban-Rad E, Nasrabadi AM. Artificial neural networks for bilateral prediction of formulation parameters and drug release profiles from cochlear implant coatings fabricated as porous monolithic devices based on silicone rubber. J Pharm Pharmacol. 2014 May;66(5):624-38. doi: 10.1111/jphp.12187. Epub 2013 Dec 17.
- Zhao F(1), Lu J(1), Jin X(2), Wang Z(1), Sun Y(1), Gao D(1), Li X(1), Liu R(3). Comparison of response surface methodology and artificial neural network to optimize novel ophthalmic flexible nano-liposomes: Characterization, evaluation, in vivo pharmacokinetics and molecular dynamics simulation. Colloids Surf B Biointerfaces. 2018 Dec 1;172:288-297. doi: 10.1016/j.colsurfb.2018.08.046. Epub 2018 Aug 23.
- Lee Y(1), Khemka A, Yoo JW, Lee CH. Assessment of diffusion coefficient from mucoadhesive barrier devices using artificial neural networks. Int J Pharm. 2008 Mar 3;351(1-2):119-26. doi: 10.1016/j.ijpharm.2007.09.032. Epub 2007 Sep 29.
- Baba H(1)(2), Takahara J(3), Yamashita F(4), Hashida M(4)(5). Modeling and Prediction of Solvent Effect on Human Skin Permeability using Support Vector Regression and Random Forest. Pharm Res. 2015 Nov;32(11):3604-17. doi: 10.1007/s11095-015-1720-4. Epub 2015 Jun 2.
- Yang X, Wang Y, Byrne R, Schneider G, Yang S. Concepts of Artificial Intelligence for Computer-Assisted Drug Discovery. Chemical Reviews. 2019 Sep 25; 119(18): 10520-10594. doi: 10.1021/acs.chemrev.8b00728.

- Paul D, Sanap G, Shenoy S, Kalyane D, Kalia K, Tekade RK. Artificial Intelligence in Drug Discovery and Development. Drug Discovery Today. 2021 Jan; 26(1):80-93. doi: 10.1016/j.drudis.2020.10.010.
- Patil KS, Hajare AA, Manjappa AS, et al. Design, development, in silico and in vitro characterization of Docetaxel-loaded TPGS/ Pluronic F108 mixed micelles for improved cancer treatment. Journal of Drug Delivery Science and Technology, 65, 2021, 10268, https://doi.org/10.1016/j.jddst.2021.102685
- Akhondzadeh S. The Importance of Clinical Trials in Drug Development. Avicenna Journal of Medical Biotechnology. 2016 Oct-Dec; 8(4):151. PMID: 27920881; PMCID: PMC5124250
- Zhong F, Xing J, Li X, Liu X, et al. Artificial intelligence in drug design. Sci China Life Sci. 2018 Oct;61(10):1191-1204. doi: 10.1007/s11427-018-9342-2
- Awwalu, Jamilu, et al. Artificial Intelligence In Personalized Medicine Application of AI Algorithms in Solving Personalized Medicine Problems. International Journal of Computer Theory and Engineering. 2015 Dec.; 7(6), 439-443. doi: 10.7763/ijcte.2015.v7.999
- Lee JW, Maria-Solano MA, Lan VTN and Yoon SC. Big Data And Artificial Intelligence (AI) Methodologies For Computer-Aided Drug Design (CADD). Biochemical Society Transactions. 2022 Feb.; 50 (1): 241–252. doi: https://doi.org/10.1042/BST20211240
- Basile AO, Yahi A, Tatonetti NP. Artificial Intelligence for Drug Toxicity and Safety. Trends in Pharmacological Science. 2019 Sep; 40(9):624-635. doi: 10.1016/j.tips.2019.07.005
- Vokinger KN, Gasser U. Regulating AI in Medicine in the United States and Europe. Nature Machine Intelligence. 2021 Sep; 3(9):738-739. doi: 10.1038/s42256-021-00386-z.
- Tormay P. Big Data in Pharmaceutical R&D: Creating a Sustainable R&D Engine. Pharmaceutical Medicine. 2015; 29(2):87-92. doi: 10.1007/s40290-015-0090-x.
- Barry, B. W. (2001). *Novel mechanisms and devices to enable successful transdermal drug delivery*. European Journal of Pharmaceutical Sciences, 14(2), 101–114. https://doi.org/10.1016/S0928-0987(01)00167-1

- Honeywell-Nguyen, P. L., & Bouwstra, J. A. (2005). Vesicles as a tool for transdermal and dermal delivery. *Drug Discovery Today: Technologies*, 2(1), 67–74. https://doi.org/10.1016/j.ddtec.2005.05.002
- Pathan, I. B., & Setty, C. M. (2009). Chemical penetration enhancers for transdermal drug delivery systems. *Tropical Journal of Pharmaceutical Research*, 8(2), 173–179. https://doi.org/10.4314/tjpr.v8i2.44526
- Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. *Nature Biotechnology*, 26(11), 1261–1268. https://doi.org/10.1038/nbt.1504
- Mak, K. K., & Pichika, M. R. (2019). Artificial intelligence in drug development: present status and future prospects. *Drug Discovery Today*, 24(3), 773–780. https://doi.org/10.1016/j.drudis.2018.11.014
- Shameer, K., Johnson, K. W., Glicksberg, B. S., Dudley, J. T., & Sengupta, P. P. (2018). Machine learning in cardiovascular medicine: are we there yet? *Heart*, 104(14), 1156–1164. https://doi.org/10.1136/heartjnl-2017-311198
- Topol, E. J. (2019). High-performance medicine: the convergence of human and artificial intelligence. *Nature Medicine*, 25(1), 44–56. https://doi.org/10.1038/s41591-018-0300-7
- Gupta, M., Kesarla, R., & Omri, A. (2020). Role of machine learning in pharmaceutical product and process optimization. *Artificial Intelligence in Medicine*, 103, 101792. https://doi.org/10.1016/j.artmed.2020.101792
- Patel, R. P., Parikh, R. H., & Mandal, S. (2021). Application of artificial neural networks in development and optimization of drug delivery systems. *Current Drug Delivery*, 18(1), 42–51. https://doi.org/10.2174/1567201817666201009115806
- Alsulays, B. B., Hussain, M. T., & Mahrous, G. M. (2022). Design of experiments (DoE) and machine learning tools in pharmaceutical formulation development. *Saudi Pharmaceutical Journal*, 30(6), 707–715. https://doi.org/10.1016/j.jsps.2022.04.003