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Artificial Intelligence in Smart Drug Delivery Systems: A Step Toward Personalized Medicine

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Abstract

One of the most interesting applications of artificial intelligence is in the design of drug delivery systems. Smart drug delivery systems can transfer drugs to specific tissues and cells, enhancing therapeutic effects while reducing undesirable side effects. The attention will be focused on the main concepts and techniques of AI such as machine learning, deep learning, and genetic algorithms. In addition to this, genetic algorithms can be used for the selection of the best numerical models, able to predict biological processes or optimize the activity of new drugs. Besides the powerful impact of AI on drug design, its combination with new biotechnologies for personalized medicine, sometimes called theragnostic, novel diagnostic tools together with targeted therapy could ensure quality and effectiveness during the clinical research of new drugs. Artificial intelligence (AI) techniques are finding their application in almost all disciplines, with special success in healthcare. AI-based algorithms can solve complex problems related to diagnosis, prediction, control, and prevention of diseases that are beyond the scope of human abilities. At the same time, the Internet of Things (IoT) revolution has added value to the healthcare sector. The resulting combination of IoT and AI platforms presents a promising fusion to provide healthcare delivery innovations like digital drug delivery, online healthcare consultancy platforms, and virtual healthcare assistants.

In other hand personalized medicine is well-suited, regardless of potential disadvantages, for creating drug delivery systems that can respond to the exact needs and other special requirements of the patients. The development of smart drug delivery systems is a potential response to the unimodal properties of drugs and the discordance between patient requirements and the patient

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outcomes achieved by currently prescribed medications. The potential and actual positive economic and health-related impacts of advanced drug delivery technologies have created a strong demand for new advanced delivery forms.

Key Words: Artificial Intelligence, Smart Drug Delivery Systems, Personalized Medicine, Tailored medicine, Machine learning, Deep learning, Natural language processing (NLP)

1. Introduction

Over the years, traditional drug delivery systems have been developed based on specific needs to deliver therapeutics in an effective and safe manner. A collection of such methods is already available as marketed products, which can be generally placed in one of the following groups: **a)** oral or transdermal delivery systems, **b)** injectable systems, **c)** inhalation or topical creams or ointments, **d)** partially or totally bio adhesive systems, **e)** nanoscale drug delivery systems, and **f)** controlled release systems [1]. However, despite the clinical successes of the marketed products, traditional drug delivery methods possess several limitations that are particularly noteworthy for proteins and nucleic acids. Proteins have complex 3D structures that allow them to perform their specific functions, and these proteins must be administered as active agents to the patients because these molecules cannot be synthesized by human cells after administration. A variety of factors can compromise the activity of therapeutic proteins, such as proteolysis, aggregation, or denaturation.

1.1. Emergence of personalized medicine and its significance

The principle underlying personalized medicine is the capability to create therapies that are more precise and effective by identifying genetically distinct patients who can achieve improved efficacy [2]. Genome-scale measurements of biological processes in patients can recognize differences in the structure of complex diseases and predict whether a disease will benefit from a particular treatment [3]. As a result, genomic information can be utilized to better comprehend susceptibilities and strengths. This allows for early identification of those factors that provide higher probabilities of effective treatment [4]. Furthermore, these factors can be employed to help patients determine the best courses of action. The effect can be greater efficacy and decreased adverse reactions in patient care. However, personalized medicine not only encompasses the

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medical field but also multiple other fields, including diagnostics, pharmaceuticals, and the delivery of medicine. With the development of advanced technology, the prevention and even prediction of adverse drug-related health issues are possible [5]. In contrast to one-size-fits-all therapeutic designs, personalized medicine can offer new medicines adaptable to the needs of distinct patient groups. The delivery of new drug products can range from changes in formulation to complementary diagnostic tools that could be part of the therapy of various physicians. With significant implications for medical practices and the healthcare system, this technology provides the potential for early implementation [6].

AI is a transformative tool, and it can help modernize several aspects of the healthcare sector, from drug discovery to different aspects of clinical work[7]. The role of AI in personalized medicine is vital, since the advent of genomics and other omics has created a monstrous amount of data, which is way beyond the scope of traditional statistical methods to process[8]. The ability of AI to identify patterns in vast amounts of data makes it the most suitable for personalized medicine, which requires analyzing patients' genetic and clinical data to diagnose, treat, and even predict the risk of certain diseases [9]. In general, AI can assist in the development and efficient operation of personalized medicine by integrating different data types, which include clinical data, medical imaging data, omic data, etc., and by providing patient stratification, diagnostics, and highly targeted treatment to bring about successful patient outcomes[10]. Data integration helps to provide insights for targeted therapies. AI models trained on large, diverse datasets are useful in providing treatment for all patients with different disease risks, as AI-driven tools can take into consideration all possible traits of a disease and the genetic makeup of an individual[11].

Also, AI-driven machine learning models can be trained on omics data to improve predictions of drug response and prognosis and will be superior in terms of reducing the number of patients required for clinical trials and for cost reductions [12]. Requirements for data privacy are few in medical diagnostics, which can be shared for the development of public tools to diagnose rare diseases and conditions. Many believe that AI plays a decisive role in a multitude of fields. In medicine, AI finds areas of complex problem-solving where expert decision-making is combined with diagnosis in areas such as radiology and pathology, where findings are from representations like images, sounds, or texts [13]. Analysis of radiological images of several different body parts highly benefits from deep learning models, which learn features and diagnose diseases automatically. The design and development of decision support systems to

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assist in radiology is a major force behind AI research [14]. The advantages of using AI in the healthcare sector are widely accepted, and opportunities and challenges for researchers are identified. AI methods have shown enormous capacities to improve healthcare areas, ranging from planning treatments for chronic diseases, psychiatric disorders, modeling and predicting diseases, fighting against rare diseases [15]. Its potential to revolutionize medicine and greatly improve human health should be widely recognized, and researchers should carefully examine which techniques of AI merit further exploitation and serious consideration for widespread clinical use.

2. Overview of AI Technologies

2.1. Tools for AI Technologies:

2.1.1. Machine learning (ML)

Machine learning (ML) is a subset of artificial intelligence (AI), associated with models that can be trained to make predictions or decisions without being specifically programmed for each case. One of the most widely used ML paradigms is supervised learning, which involves training a model to associate a certain input with a certain output. Unsupervised learning, meanwhile, aims to infer a function that can describe hidden structures of data characterized only by input features. Several ML models have been widely experimented with in the life sciences field; among these are random forests, support vector machines, and artificial neural networks (NN) [16]. Nowadays, whereas the name of some ML models, such as deep learning, has been widely used by the media, a different nomenclature, such as deep feedforward neural networks or deep convolutional neural networks, is employed in specialized literature [17].

Deep learning (DL) can also be categorized as a subtype of ML and can be applied to a wide variety of domains [18]. DL is, in fact, an algorithm that allows ML to make decisions, executing a series of functions using parameters learned from large amounts of labeled data and employing simple modules like the ones inspired by the function and structure of the human brain [19]. Different deep learning models may be more useful when treated with specific kinds of data or tasks [20]. Deep feedforward neural networks have a simple three-layer architecture (input, hidden, and output), characterized by the absence of cycles and a virtually unlimited number of units, which may be used to model intricate relationships [21]. A recurrent neural network (RNN) is another popular DL model that can capture patterns and trends in sequential data, which makes

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it a useful resource, especially in time series prediction [22]. The transformer, which behaves similarly to an RNN model but has no limiting structures that confine information propagation in time or space, has been applied in document sound and language modeling, as well as in serving models for question-and-answer platforms [23].

2.1.2. Deep learning (DL)

Deep learning, as a subfield of AI, provides an efficient and robust mechanism for modeling and approximating complex data by processing a large-scale, high-dimensional feature set through varying degrees of flexible deep multilayer structures with many easily tunable parameters [24]. In contrast to analogical models based on advanced linear algebra, the structure in deep learning allows for the construction of end-to-end systems for learning from massive and unfiltered data [25]. As a result, deep learning offers great potential in revolutionizing medical imaging and bioinformatics data analysis for both fundamental research and clinical diagnosis. The goal is to build automatic, reliable, and interpretable assistant tools to reduce human labor and dissatisfaction in weak AI realization over time [26].

Despite the success of deep learning in other fields, its application in biomedicine often encounters methodological and theoretical challenges due to the high cost of labeled data, low cost of high-throughput data, and corresponding highly variable quality of molecular bio profiling results, intrinsic sample variability in human subjects, and ethical constraints of animal studies [27]. For example, the signal of complex annotations from different pathophysiological processes sampled at different spatial locations and temporal stages in medical imaging data incurs high false positive and false negative risks due to semantic mismatch. Multiple variables from different animal cohorts or subjects impose a burden on experimental design [28]. Biological event-derived conditions often suffer from intrinsic distribution shift problems due to the confounding effects of both the among-subject and within-subject cycles of multiple observations. These challenges lead deep learning method developers to focus not only on new, well-generated interpretable models from various perspectives but also on robust, adaptively and transparently robust models with controllable parameters for custom adaptation and model calibration through novel theoretical perspectives[29].

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2.1.3. Natural language processing (NLP)

Natural Language Processing (NLP) is a branch of artificial intelligence aimed at training machines to understand, interpret, and process human languages. In the context of personalized medicine, the intersection of NLP and AI can be particularly valuable [30]. Combining insights into clinical data can help form clusters of patients based on characteristics such as economic status, age, geographical area, and other socioeconomic parameters [31]. Another example of the NLP application suggests taking into consideration not only descriptions of disease genomics but also text-based EHR data, such as the description of pathology results, reports of imaging tests, nurse notes with medical care information, or descriptions of lifestyle from doctors or psychologists [32].

Knowledge discovery in clinical notes is associated with the creation and use of tools and methodologies for examining clinical notes to find new information about patients, diseases, or treatments [33]. When it comes to customizing care plans that are right for unique patients, obtaining scientific knowledge is key. It is vitally important for businesses to build powerful, efficient NLP approaches to realize the promise of Big Data in delivering knowledge from unstructured EHR data [34]. With the advancement of EHRs, we have the chance to finally obtain actionable knowledge from large-scale clinical notes. The increasing number and consistency of patient-encounter records combined with EHR popularity have allowed many studies to be conducted, establishing principles and techniques, and many helpful applications using clinical notes as research topics. Sharing data availability and such resources can help transform future patient care [35] [36].

2.1.4. Neural networks (NN)

NN is the most important modeling tool in modern artificial intelligence. It consists of massive numbers of neuron-like units. Each unit receives input and has the capacity to generate output through a function. Input to each unit is a weighted sum of all signals received by all units in the previous layer [37]. Every input is then multiplied by a weight proposed by an algorithm, and then the weighted sum is input into a nonlinear transformation or activation function proposed by an algorithm. As a result of the nonlinearity introduced by the neuron model, it is possible to build a system with a generic decision-making system that can model very complicated patterns with an arbitrary degree of complexity[38]. It is considered the most useful

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tool in solving machine learning problems. The methodology can automatically detect complex patterns from raw data and is useful for making predictions, classifications, time-series modeling, image and data compression, etc [39]. In the healthcare sector, the extraction of such useful patterns is important in disease detection, prediction, diagnosis, treatment, device and drug development, and clinic planning, etc. NN is also extensively used in bioinformatics, clinical data analysis, and health informatics.

In the pharmaceutical industry, package and prescribing errors can be prevented through machine learning that deploys NN for clinical decision-making. For successful diagnosis and efficient prognosis of different diseases, brain-computer interfaces, analysis of blood, endoscopies, heart and lung tones, skin, etc. [40]. NN is capable of learning about individual patient medication. Input information, e-prescribing was positioned and optimized to provide appropriate and essential care for long-term, acute-care survival patients. In addition, neural learning will effectively categorize health data that address frequent disease types and provide efficient and essential healthcare solutions during outbreaks like health crises, which potentially occur at a record rate[41].

2.2. The Role of ML, NLP, and Deep Learning in Data Denoising

The realm of data denoising has witnessed a transformative evolution through the advent of various technologies, each contributing unique methodologies and insights. The term "denoising" itself evokes a process reminiscent of clarifying a muddled message, akin to distilling the essence from noise. In the landscape of machine learning, myriad algorithms have emerged, designed to sift through data clutter with remarkable precision. Machine learning (ML), a cornerstone of contemporary data science, has redefined the parameters of data analysis. By leveraging intricate patterns within datasets, ML techniques enable the identification and removal of anomalies that obscure clarity. Natural language processing (NLP), another critical component, extends this paradigm to textual data, employing linguistic models to refine and enhance the quality of communication [42]. Here, the focus lies on eliminating syntactical noise and semantic ambiguities, paving the way for more coherent interpretations. Moreover, neural networks have taken the forefront in this endeavor, functioning as intricate webs of interconnected nodes that emulate human cognitive processes. These networks are adept at learning from vast quantities of data, making them invaluable for denoising tasks that require

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deep contextual understanding [43]. Deep learning, a subset of this technology, further amplifies these capabilities, allowing for the extraction of features at multiple levels of abstraction. This layered approach facilitates the discernment of subtle signals amidst the cacophony of irrelevant information. In summary, the convergence of machine learning, natural language processing, neural networks, and deep learning has forged a robust framework for the denoising of data. Each technology contributes its distinctive strengths, collectively enhancing our capacity to achieve clarity and precision in an increasingly complex data landscape [44].

Table 1. An overview of software platforms that speed up different phases of the drug research and discovery process by utilizing AI techniques including deep learning, predictive modeling, and virtual screening

Software	Interpretation	Characteristics	Ref
DeepMind AlphaFold (Google, Mountain View, CA, USA) https://deepmind.google/technologies/alphafold/, accessed on 10 October 2024	protein structure prediction by Deep learning model	Forecasts protein structures with high accuracy	45
Atomwise (Atomwise Inc., San Francisco, CA, USA) https://www.atomwise.com/, accessed on 10 October 2024	AI-driven drug discovery platform	Virtual screening, lead optimization	45
Recursion Pharmaceuticals (Recursion, Salt Lake City, UT, USA) https://www.recursion.com/, accessed on 10 October 2024	High-throughput screening platform	Cellular phenotypic analysis, rare diseases	46
BenevolentAI (Benevolent AI, London, UK) https://www.benevolent.com/, accessed on 10 October 2024	Drug discovery and development platform	Predictive modelling, target identification	47
Schrödinger Maestro (Schrödinger, New York, NY, USA) https://www.schrodinger.com/, accessed on 10 October 2024	Molecular modelling and simulations	Molecular docking, QSAR modelling	48
Insilico Medicine (Insilico Medicine, Hong Kong) https://insilico.com/, accessed on 10 October 2024	Drug discovery and biomarker development	Generative modelling, drug repurposing, and aging research	49
XtalPi (QuantumPharm Inc., Boston, MA, USA) https://www.xtalpi.com, accessed on 10 October 2024	AI-driven drug crystal prediction	Predicts drug crystal forms, stability	50
Cyclica (Cyclica, Toronto, ON, Canada) https://cyclicarx.com/science/, accessed on 10 October 2024	AI-driven drug discovery platform	Polypharmacology prediction, target deconvolution	51

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3. Applications of AI in Drug Development

3.1. Drug discovery and design

3.2. Predictive modeling for efficacy and toxicity

3.3. Optimizing clinical trials

3.4. Other application

3.1. Drug discovery and design

There are several highly technical review articles that discuss the use of artificial intelligence (AI) in drug design, though nearly all of them are specifically targeted at algorithms or areas [52]. Here we present a brief overview of the main areas of application of AI in drug discovery and design. Central to AI in drug discovery is the concept of 'in silico drug discovery,' where the vast amounts of genomic, chemical, and pharmacological data available are used to computationally describe biological systems and chemical processes with the goal of designing and discovering new compounds of therapeutic value [53]. As a result, this technology has the potential to fundamentally change the way in which drugs for many diseases are discovered and developed[53].

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Fig 1. Application of AI in drug development

The first applications of AI in drug discovery are mostly in computer-aided drug design, such as the often-discussed docking of molecules using machine learning or molecular description and prediction using deep learning [54]. This includes the creation of libraries of chemical properties and structural information about drugs, the analysis of structural properties of drug target proteins such as proteomics research, the study of interactions between drug molecules and their corresponding endogenous protein targets such as in the determination of QSAR, enzyme-substrate interactions, and the prediction of binding constants [55]. These applications

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have a significant impact on understanding the complexity of the human genome and in proposing new biological mechanisms that could not be previously envisaged for drug intervention [56]. In silico drug discovery has also had an expanded impact on finding new indications for drugs already in the market, to propose, for example, repurposing some drugs in the treatment of cancer or in the elucidation of the off-target effects of some drugs [57 58].

3.2. Predictive modeling for efficacy and toxicity

Predictive modeling approaches, machine learning algorithms, and QSAR are widely employed for generating predictive models to integrate large amounts of data from diverse sources and types [59]. However, predicting and optimizing the efficacy of personalized drug combinations is still very challenging. Investigations directed at optimizing drug combinations predominantly focus on chemical pleiotropy and signaling pathway crosstalk [59]. However, the development of facile predictive algorithms, sophisticated systems biology models, and big data analytical approaches enables insights into a more complete set of molecular consequences of drug exposure, which could improve drug combination selection for efficacy, influence the direction of drug development, and identify potentially overlooked toxicities [60]. QSAR, pharmacokinetic models, and PBPK models have been developed to predict the joint effects of therapeutic interventions [61].

There is enormous potential for advancing precision medicine by leveraging the growing power of technology for drug combination selection through precision medicine research. This may, however, require an improved view of the nodes that mediate drug–drug interactions and expanded human data banks [62]. Logic circuits, signaling and regulatory networks, and derived decision trees can uncover the complexities of drug-induced changes and lead to the elucidation of combinations of reagent interventions. The design of novel combinations can be driven by a joint desire to minimize the probability of success while limiting adverse effects and enhancing therapeutic outcomes [63]. Machine learning can guide the joint development of the multidrug microbiome system or suggest potential novel regimens by the discordance of optimizing cancer drug combinations in cells versus xenograft mice, or by identifying drug–target–pathway connections in certain cell types. Existing experimental and bioinformatics approaches can provide the gold standard training sets for scrutiny of unexplored cells and tissues. The ideal

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learning paradigm may not exist, and multifaceted, Mult constraint workflows may be necessary for different situations.

3.3. Optimizing clinical trials

The use of artificial intelligence algorithms to select the appropriate patient population and the optimal dosing is expected to raise the rate of clinical trial success. 90% of novel anticancer compounds entering phase I clinical trials never reach the market [64]. Among these drugs, many are efficacious but just for a small fraction of patients, while most of the non-lethal side effects are not acceptable. Companies are working together to optimize trial recruitment, and several startups are involved in the AI-based selection of patients for their inclusion in clinical trials on patient-centric protocol design[65] (Table 2). Optimization of the patient cohort may also lead to improved outcomes of the clinical trial. A challenge demonstrated how the AI algorithm, as a background, leads to more accurate re-assessment of breast cancer risk. Optimized clinical trials with enriched cohorts may result in shorter trials, saving time and money, and may reduce the dropout rate due to adverse events, thus speeding up clinical development and marketing[66]. Moreover, with proven efficacy, the new therapeutic formulation or packaging option can be approved as a bioequivalent of the listed counterpart. Since the optimized patient population and very positive results can boost the price and thus profitability, investments will be easier to find while marketing expenses may be lower[67 68].

Table 2. Clinical Trial Utilizing Artificial Intelligence [69]

Trial ID (NCT/DOI)	Condition/Disease	AI Application	Purpose of AI
NCT06059378	Optical Polyp Detection	Using AI-assisted Optical Polyp Diagnosis for Diminutive Colorectal Polyps (AI-OD)	to show the accuracy of intracolonoscopy
NCT05178095	Colonic Polyp Detection	Artificial Intelligence in Colonic Polyp Detection	detection of colonic polyps during outpatient colonoscopy
NCT04358198	Gastric Intestinal Metaplasia Diagnosis	Usefulness of Artificial Intelligence (AI) for GIM	diagnosing gastric intestinal metaplasia
NCT05489471	Lung Cancer	Impact of an Artificial Intelligence (AI) System on Chest X-ray Reporting	Nodule detection and malignancy prediction

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NCT06093217	Acute Pulmonary Embolism (AID-PE) (AID-PE)	Artificial Intelligence to Improve Detection and Risk Stratification of AID-PE/ AID-PE	detection of acute Pulmonary Embolism (PE) in patients who undergo Computed Tomography Pulmonary Angiogram
NCT04918992	Pelvic Cancers	Post Radiotherapy MRI Based AI System to Predict Radiation Proctitis for Pelvic Cancers	predict radiation proctitis for patients with pelvic cancers underwent radiotherapy
NCT06456203	Respiratory Tract Infections Infections Lung Diseases Respiratory Tract Diseases Pneumonia	Trial of Artificial Intelligence for Chest Radiography (ACER)	an economic analysis of impact of AI decision support on radiology service delivery.
NCT06934239	Brest Cancer	Impact of Artificial Intelligence on Breast Cancer Screening (PRISM)	To compare patient-cantered outcomes when 3D screening mammograms are interpreted with versus without a leading FDA-cleared AI decision-support tool in real-world U.S. settings
NCT05018663	Pancreatic Solid Lesions	Artificial Intelligence (AI) Cytopathology Trial	To compare accuracy of preliminary diagnosis results between ROSE and AI at bedside versus final pathology report
NCT05241483	Laboratory Critical Values Predictive Value of Tests Reference Values Relative Value Scales Vital Signs	Remote Patient Monitoring and Detection of Possible Diseases With Artificial Intelligence Telemedici ne System (AI - diseases)	Possible disease detection with artificial intelligence from the patient's vital values possible disease detection from the patient's examination records
NCT05423964	Adenoma Adenoma Colon Colorectal Cancer	Impact of AI on Trainee ADR	To determine the impact of AI based endoscopy on the rate of recording of quality improvement metrics versus historical performance in our program.
NCT06527378	Edentulous Alveolar Ridge Edentulous Mouth	Artificial Intelligence in Dental Implant Planning (AIDENT)	offering new opportunities to improve the precision and

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	Tooth Loss		efficiency of implantology
NCT06877988	Visual Impairment	Artificial Intelligence (AI) - Assisted Visual Impairment Screening Model: Community-based Implementation and Evaluation of Performance, Feasibility and Costs.	To evaluate the performance, operational efficiency, acceptability, feasibility, and cost-effectiveness of an AI-assisted screening model for visual impairment in a community setting.
NCT06301945	Thymic Carcinoma Thymic Epithelial Tumor Thymoma Thymoma and Thymic Carcinoma	Artificial Intelligence Prediction Tool in Thymic Epithelial Tumors (INTHYM)	To improve the accuracy of histopathological classification of thymic epithelial tumors, and to better predict the risk of recurrence
NCT05438576	Cardiomyopathy Pregnancy Related	Screening for Pregnancy Related Heart Failure in Nigeria	To evaluate the effectiveness of an artificial intelligence-enabled ECG (AI-ECG) for cardiomyopathy detection in an obstetric population in Nigeria
NCT04580095	Heart Diseases	Artificial Intelligence for Improved Echocardiography	To assess the effect of artificial intelligence algorithms on image quality in echocardiography.
NCT06763952	Diabetes Vision	Leveraging Artificial Intelligence to Prevent Vision Loss from Diabetes Among Socioeconomically Disadvantaged Communities	To investigate whether a novel artificial intelligen ce-based screening strategy improves screening and follow-up care rates across race/ethnicity groups and reduces racial/ethnic disparities in screening
NCT05339750	Allergic Contact Dermatitis	Allergy Skin Patch Artificial Intelligence (AI)	To assess human and artificial intelligenc e performance in grading contact dermatitis reactions in healthy volunteers
NCT06790134	Pancreatic Diseases	Validation of an AI-Assisted Pancreatic EUS System for Training Improvement: a Prospective, Multi-Center, Randomized Trial	To verify the auxiliary role of the artificial intelligence (AI) system in pancreatic endoscopic ultrasound (EUS) scans

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NCT06584305	Body Dysmorphic Disorder	AI Screening for BDD in Aesthetic Surgery: Enhancing Safety and Outcomes (AI)	to evaluate the effectiveness of an AI-powered screening tool for Body Dysmorphic Disorder (BDD) among patients seeking aesthetic surgery
NCT05557162	Cardiac Amyloidosis	Artificial Intelligence Enhanced ECG to Detect Cardiac Amyloidosis	to assess a novel artificial intelligen ce (AI)-enabled electrocardiogram (ECG)-based screening tool for improving the diagnosis of cardiac amyloidosis (CA)
NCT06397820	Coronary Artery Disease Coronary Artery Stenosis	Relation Between AI-QCA and Cardiac PET (AI-CARPET)	To evaluate the clinical implications of artificial Intelligence (AI)-assisted quantitative coronary angiography (QCA) and positron emission tomography (PET)-derived myocardial blood flow in clinically indicated patients
NCT06412900	Kidney Stone Obstruction Ureter Renal Colic Ureter Stone	Radiomics and Image Segmentation of Urinary Stones by Artificial Intelligence (RISUS_AI)	To personalized and improved treatment and follow-up of patients with kidney stones using radiomics and the development of an artificial intelligence tool for CT examination assessment

4. Smart Drug Delivery Systems

4.1. Controlled release systems

Since pharmacokinetic parameters in drug release should be highly controlled and allowed to be determined in a certain target, applying particular drug release in the needed part of the body eliminates the inconvenience of numerous drug administrations, enhances simple structure therapy, and guarantees patients' compliance[70]. This is the creation of controlled release systems. Artificial intelligence methods and control theory are gaining increasing recognition, and their implications in this direction have grown vastly. These critical observations propose a more intensive impact of the interdisciplinary strategy in solving the

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extremely practical challenges inherent in this subject. Some challenging points of drug pharmacokinetics, dynamics, and modeling that are enhanced or limited by incorporating specific processes or applications are presented [71]. Controlled release systems or multiple dosing regimens are self-associative, crystalline, polycrystalline, amorphous, and microporous drug carriers, drug-polymer conjugates, osmotic and electronic pumps delivering drugs, which possess a particular pharmacokinetic and pharmacodynamic profile. These profiles could be different from those produced by established prolonged-action drugs and have a similar range of therapeutic effects [72]. The pharmacokinetic and pharmacodynamic times of such drug exposure should be determined in a certain target. Then, to be of interest, controlled release dosage forms might reasonably affect certain changes in the pharmacokinetic and pharmacodynamic processes [73]. A specific controlled release involves stopping the drug release, drug reprocessing, and adaptation of the most important actions. Such research, development, and production of controlled release systems have focused great interest in this subject.

4.2. Targeted delivery mechanisms

The precise identification of suitable targets using an appropriate molecular recognition system, and the release of active therapeutic agents in the right dose at the right place, is a crucial feature of any practical smart drug delivery system [74]. Nanoparticles designed for use in vivo can also incorporate targeting moieties that recognize and interact specifically with certain cell types or structures. The function of the tissue/cell-specific ligand on the nanoconstruct is to confer cell-specific properties to the nanoconstruct, allowing it to selectively target and accumulate in its target location. Ligands also reduce the uptake of nano constructs by tissues not constitutively expressing the target antigen. Such ligands reduce the level of nano construct accumulation in less-targeted tissues while increasing the circulation of the particles in the body [75]. This interaction can improve the resolution in the delivery of the drug and allow its controlled release with minimum side effects. Overall, the use of ligand-targeted nano constructs in vivo results in improved drug delivery and drug efficacy at the targeted site[76] [77].

A guideline block of text in a column of scientific literature shows that in vitro and in vivo studies report that targeted delivery systems improve delivery and uptake. However, researchers have variously referred to different materials, structures, and configurations, as well as ligand attachment methodologies. A comprehensive and systematic survey is required, using

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advanced information collection techniques and scientific knowledge discovery methods[78]. Such a study will provide researchers with a broad perspective on which particles or systems are often mentioned, why, and to what extent nanomaterial ligand attachment influences the property and function in these works. This study will enable researchers to grasp the current research status and to identify further research needs[79]. Such a study in relation to smart drug delivery systems is a key reason for conducting the proposed work. Users can find out which systems are often machine-readable, which molecules are attached and get an overview of the techniques currently in use [80].

4.3. Bio-responsive systems

The design of stimuli-responsive or bio-responsive systems could be seen as an intelligent approach to deal with the drug delivery challenge. A general strategy aims to locally apply energy to control release kinetics, elimination, or spatial resolution [81]. The use of, for example, light, sound waves, magnetic fields, or variations in temperature has been reported. Phototherapy methods currently play a significant role in the treatment of cancer [82]. Hence, a local energy impulse could trigger the response to the dose of an applied therapeutic or supporting agent. Besides photodynamic therapy, the use of types of particles could be strongly promising towards photothermal and/or sonodynamic therapies [83]. Moreover, upon such a locally applied set of external conditions, some smart liposomes and polymeric carriers could undergo subsequent transformations, enhance their encapsulating potentials, or release the loaded agent [84].

While designing those smart nanocarriers,[85] the approach of "planning for a long time of operation, considering many possible target molecules for action as much as possible," as seen from the point of view of the number of functions per system established, seems just a "pure science" overstatement for an engineer, less updated towards the realistic range of opportunities awaiting medical use [86]. In this sense, the use of these smart nanocarriers as hosts for therapeutic agent functions requiring some substitution of defective proteins and cell functions using different types of oligomers and polymers could represent a promising groundbreaking use concerning personalized medicine applications [87].

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5. AI-Driven Innovations in Drug Delivery

5.1. Predictive analytics for formulation design

Machine learning has seen a surge in popularity of research in study formulation design in recent years as it can enable rapid and high-throughput material discovery due to improved prediction accuracy of AI models [88]. Further, this approach allows customization of drug delivery systems (e.g., tailoring release rates, increased stability which can prolong drug shelf life). In one example, a formulation design software has been implemented to innovate drug-loaded nanostructured lipid carriers with the desired spray drying characteristics, drug encapsulation, and drug release profiles for application in dry powder inhalation [89]. Using this software to optimize NLCs for dry powder inhalation enabled greatly enhanced depositing aerosol and increased dissolution rate. This transformative approach will enable a personalized, adjustable drug release system tailored to each patient's unique macromolecular composition for the treatment of various drug indications as we unravel new drug distribution mechanisms and develop reliable predictive capabilities [90] [91].

In another example, a unified adaptive design optimization of an mRNA-based vaccine formulation was described that would cover the whole vectorial/combinatorial composition space of an mRNA formulation in as few labs experiments as possible [92]. The model search technique was then applied to find the most efficacious personalized mRNA vaccine formulation. Follow-up wet lab characterization experiments validated the model predictions. In this work, the personalized process would rule out all specific antigens, enable evaluation of a large pool of candidates for all respondents by delivering a personalized mRNA vaccine to all participants [93]. Although these studies have demonstrated the potential of predictive analytics for drug formulation design and material discovery, it is important to stress that there are still major challenges in overcoming 1) obtaining high-quality data and models, 2) how to transfer models across settings and into the clinic, and 3) the cost of goods sold necessary to implement AI-guided strategies into a living cell or establishing the recommendations and quality standards for regenerative medicine [94].

5.2. Optimization of dosage and release profiles

To ensure that the administered dose of a drug is the most efficacious, it is often necessary to tightly control the release kinetics of the drug cargo. Parenteral routes of

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administration for most drugs deliver a constant, low-dose background level, with a bolus of additional drug after administration [95]. This may not be a biologically relevant mimic of the peak-and-trough release profile for orally administered drugs, leading to inefficient drug utilization and a risk of adverse effects. Therefore, for many drugs, it would be beneficial to develop formulations with release kinetics that better mimic those of non-parenteral routes of administration [96]. Optimization of complex drug-release profiles has already been demonstrated using proof-of-concept setups and algorithms, showing the potential for reduced time-to-market, money, time, and waste in the development of proposed formulations with desired release profiles [97].

Tailoring the release profile of a given therapeutic compound over time to deliver the drug most effectively and efficiently is of high relevance and interest, offering a fascinating combination of goal-driven research, challenges [98]. Exploration of AI-based systems can be expected to lead to innovative and, most probably, unconventional solutions. In this review a brief overview of how AI is currently used to actively optimize the dosage and release profiles of existing drug delivery systems, as well as to develop new drug delivery systems that can be used to optimize the release profiles of known therapeutic compounds for any given effect specification [99]. It must be considered the optimization of active pharmaceutical ingredients within current mainstream dosage forms, followed by an exploration of how AI can be theoretically extended to the design and optimization of non-parenteral, nonoral drug delivery systems that offer the possibility of unique release profiles, rivaling or augmenting those which result from initial drug discovery, thereby offering the possibility of eliciting novel drug effects[100].

5.3. Integration with nanotechnology and biosensors

The development of various artificial intelligence (AI) techniques has its own roots entangled with the specialized disciplines within nanotechnology such as nanomaterials, nanoelectronics, nanobiotechnology, and nanocomputing [101]. On the other hand, AI integrated with nanotechnology is the formulation of AI-driven nano techniques consisting of AI-based modeling, synthesis, characterization, testing, and quality control. AI can create thinking machines that could simulate biological neurons. Nano biocomputing systems include memory,

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processors, and others that are dedicated to the consistent performance of computing within bioinformatics.

AI, integrated with medical research and the administration of drugs, also plays a pivotal role in the field of pharmacy. For several years, research and studies have been evolving with the perfect match of AI and nanotechnology, which has ushered in the design and fabrication of nanoparticles, exploiting the intrinsic properties of the nanostructured material [102]. Most of the work has been concentrated on the drug delivery of spare material. At the same time, some of the work is focused on the targeted distribution of biofunctionalized nanoparticles for cancer treatment and diagnostic imaging [103].

Table 3. Popular AI model tools used for drug discovery [89] [104] [105] [106] [107].

AI Model Tools	Summary	Application Area	Example / Use Case
DeepChem	Deep learning models for molecular property p rediction, virtual screening, and generative che mistry are among the many tools and models f or drug development offered by this open-source library.	Predictive modeling, QSAR, multitask learning	Predicting bioavailability and solubility in nanoparticle drug formulations
RDKit	A popular open-source cheminformatics library with a number of features including handling molecules, searching substructures, and calculating descriptors. Drug discovery software can incorporate it with machine learning methods.	Molecule manipulation, descriptor calculation	Generating molecular fingerprints for drug-likeness evaluation
ChemBERTa	A conceptual model developed especially for tasks involving drug development. It can produce molecular structures, predict characteristics, and aid with lead optimization because it is pre-trained on a sizable corpus of chemical and biomedical literature and is based on the Transformer architecture.	NLP-based molecular property prediction	Predicting ADMET properties from SMILES without handcrafted features
GraphConv (Graph Convolutional Models)	A molecular graph-based deep learning model architecture. By using the structural information contained in the graph representation of molecules, it has proved successful in forecasting molecular characteristics like toxicity and bioactivity.	Structure-based prediction of drug activity	Predicting IC50 of drugs on cancer cell lines using molecular graphs
AutoDock Vina	A well-known docking program that predicts the binding affinity between small compounds and protein targets using machine learning approaches. It can help with lead optimization and virtual screening for drug discovery.	Molecular docking and virtual screening	Identifying drug candidates for COVID-19 main protease

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SMILES Transformer	A deep learning model that creates molecular structures from Simplified Molecular Input Line Entry System (SMILES) strings. Lead optimization and de novo drug design are two applications for it.	Molecular representation learning (NLP)	Pretraining on SMILES for generative drug design and property prediction
Schrödinger Suite	A complete drug discovery software suite that includes a number of AI-powered capabilities. Predictive modeling, ligand-based and structure-based drug design, virtual screening, and molecular modeling are among its modules.	Molecular dynamics, docking, binding affinity	Simulation of protein-ligand complexes for kinase inhibitors
IBM RXN for Chemistry	An artificial intelligence model for chemical reaction prediction. It helps with drug synthesis and the development of new synthetic pathways by generating possible reaction outcomes using deep learning algorithms and sizable reaction databases.	Reaction prediction, synthesis planning	Designing retrosynthesis pathways for custom prodrugs
scape-DB	A database called scape-DB (Extraction of Chemical and Physical Properties from the Literature-DrugBank) uses machine learning and natural language processing to extract biological and chemical information from scholarly publications. It offers useful data for studies on medication discovery.	Scaffolding and bioisosteric replacement	Identifying alternative scaffolds for known therapeutic compounds
GENTRL (Generative Tensorial Reinforcement Learning)	A deep learning model that creates new molecules with desired characteristics by fusing generative chemistry and reinforcement learning. De novo drug design and optimization have made use of it.	Generative molecule design with reinforcement	Designing novel opioid analgesics with desired potency and low abuse potential
Genetic Algorithms	Genetic algorithms are optimization methods that draw inspiration from the concepts of genetics and natural selection. To obtain the required dosage form properties, they can be used to optimize formulation compositions, drug release patterns, and process parameters.	Feature selection, formulation optimization	Optimizing nanoparticle composition for sustained release
Artificial Neural Networks (ANNs)	Drug release kinetics from various dose forms have been modeled and optimized using artificial neural networks (ANNs). They can help identify the best formulations and forecast how active pharmaceutical ingredients (APIs) will release under different circumstances.	QSAR, release profile prediction	Predicting release rate of drugs from hydrogels based on polymer properties
Support Vector Machines (SVMs)	To forecast and model interactions between formulation variables, including excipient composition, processing parameters, and drug release profiles, SVMs have been employed in dosage form optimization. They facilitate formulation design space optimization.	Classification of active/inactive compounds	Predicting drug-likeness and toxicity of new compounds
Particle Swarm Optimization (PSO)	For the purpose of optimizing dose forms, PSO is a population-based optimization algorithm. It has been used to optimize dissolution profiles,	Parameter optimization, hybrid modeling	Optimizing ANN weights for drug release modeling

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	particle size distribution, and other formulation factors.		
Artificial Intelligence-based Expert Systems	Expert systems mimic human experts' decision-making processes by using AI approaches such as fuzzy logic and rule-based systems. Taking into account various formulation and process variables, they can be used for dosage 44form optimization.	Decision support for formulation & synthesis	Recommending excipient selection for personalized oral dosage forms
Monte Carlo Simulation	By taking into account the uncertainties and variability in formulation and process factors, Monte Carlo simulation techniques have been utilized to optimize the performance of drug products. They support process design and strong formulation.	Probabilistic modeling, pharmacokinetics	Modeling absorption variability in transdermal drug delivery
Computational Fluid Dynamics (CFD)	The optimization of fluid flow and mixing in dosage form production processes, including granulation, coating, and drying, is made possible by CFD models. They aid in the creation of consistent and effective procedures.	Simulating drug transport in biological systems	Modeling blood flow-mediated drug delivery in microvessels
Response Surface Methodology (RSM)	Through the modeling and analysis of the interaction between various variables and their impact on formulation responses, RSM is a statistical technique that aids in the optimization of dosage form formulations. It facilitates comprehension and formulation parameter optimization.	Experimental design, formulation optimization	Optimizing liposomal formulation for maximal entrapment efficiency
Artificial Neural Network–Genetic Algorithm (ANN-GA) Hybrid Models	To optimize dose forms, hybrid models that combine ANN and GA approaches have been utilized. To find the best solutions and forecast formulation properties, they can effectively search the formulation space.	Release kinetics modeling, optimization	Modeling and optimizing in situ gel formulations for ocular drug delivery
Multivariate Analysis Techniques	Dosage form optimization has made use of multivariate analysis techniques including partial least squares (PLS) and principal component analysis (PCA). They help with dimensionality reduction, formulation performance optimization, and the identification of crucial formulation factors.	Chemometrics, PCA, PLS for data reduction	Analyzing HPLC profiles of drugs for quality control

6. AI Applications in Implantable Drug Delivery Devices

6.1. Role of feedback mechanisms

A significant aspect associated with the systems encompassing artificial intelligence is feedback. In systems driven by data, the importance of feedback is significantly amplified. The inclusion of feedback in smart delivery systems would allow the dose and frequency of agent

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administration to be adjusted according to individual characteristics and dosing targets, thus improving therapeutic effects, reducing toxicities, and minimizing ADR risks [108]. The use of feedback in systems necessitates a shift away from the self-healing systems described previously in favor of prescribed healing mechanisms. This reliance on prescribed healing mechanisms necessitates the use of responsive materials and devices [109]. Materials responsive to various stimuli, ranging from environmental factors to those associated with the therapeutic target, hold promise for incorporating feedback into the drug release mechanism. Such a development would demand the convergence of material chemistry, responsive polymers, responsive amphiphiles, and responsive composite materials, such as pH-responsive nanoparticles. Additionally, appropriate devices and assembly techniques capable of altering drug dose delivery rates or switching drug release on and off would need to be engineered with a high degree of precision [110]. Research in responsive polymers and pharmaceutical excipients is classified as responsive materials relevant to drug release modulation. Drug delivery systems featuring good flexibility in the modulation of agent release patterns, such as drug-eluting stents, can incorporate both iontophoretic and transport machine feedback schemes [111]. These advanced smart drug delivery systems can revolutionize current clinical practice by virtue of their capability to offer therapeutic doses of the drug in response to the real needs of the patient, without demanding the patient to be physically treated in a hospital.

6.2. Adaptation to patient-specific requirements

Pharmacological treatment in drug delivery design is typically delivered in fixed doses to patients of variable physio pathological characteristics. For instance, patients may exhibit distinct disease progressions, such as slowed vascular blood flow in the vicinity of cholesterol plaque deposits in the context of inflammatory macrophage recruitment for atherosclerosis, which can affect the preferred particle type, size, coating chemistry, and site of release [112]. Another aspect is the complex interaction of particle properties with the human body, from the protein corona that forms upon injection to the targeting and transportation capabilities that are dictated by the complex biological forces that control particle-particle and particle-tissue interaction. Together, this implies that a personalized approach toward particle design will become ever more relevant as we strive to treat patients in the most non-toxic, cost-effective, and successful manner [113]. AI can significantly aid this development by capturing and utilizing

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vast amounts of knowledge of existing drug delivery systems, either used in their target context or in various other applications [114].

7. The Concept of Personalization in Medicine

7.1. Genetic and phenotypic considerations

Genetics essentially determines not only the physiological and behavioral traits of an individual but also their propensity to develop diseases. The knowledge of specific genetic information may be pivotal for therapeutic decisions at an individual level [12]. Pharmacogenetics and genotyping have already shown promise in individualized drug treatment by identifying genetic links to variations in therapeutic response to drugs. The defining elements associated with drug metabolism and individual-to-individual differences in targets such as drug receptors offer the ability to tailor treatment regimens with the greatest likelihood of positive benefits and reduced likelihood of toxicity due to drugs. The inherited genetic information describes only a portion of drug response, and additional factors like diet, the microbiome, acquired genetic information, disease status, concomitant medication, and pharmacoeconomic issues can have substantial effects on drug response[115].

Personalization, based on a variety of phenotypic and genotypic assessments, is the advance of present drug selection strategies. Single nucleotide polymorphisms (SNPs) alter the response of some drugs and thus should influence several drug treatments in clinical practice [116]. The role of SNPs in terms of linking specific drugs to specific diseases has not yet been fully appreciated. Pharmacogenetics is defined as the research of all inherited factors that affect drug actions in families and populations. The association of genotypic differences with inter-individual fluctuation in drug efficacy and toxicity outcomes is also known [117]. Through analyzing genetic variation, we plan for a personalized medicine approach and convey the right dose and the correct drug to the right patient. In terms of inherited factors as well as prior genetic illnesses and other positive characteristics important for medical decisions such as disease diagnosis, clinical evaluation, and gene function evaluation, pharmacogenetics has evolved significantly [118]. The analysis of the genetic variants influencing the reaction to a medication may be realized through both genome-wide association studies and clinical pharmacogenetics implementation [119].

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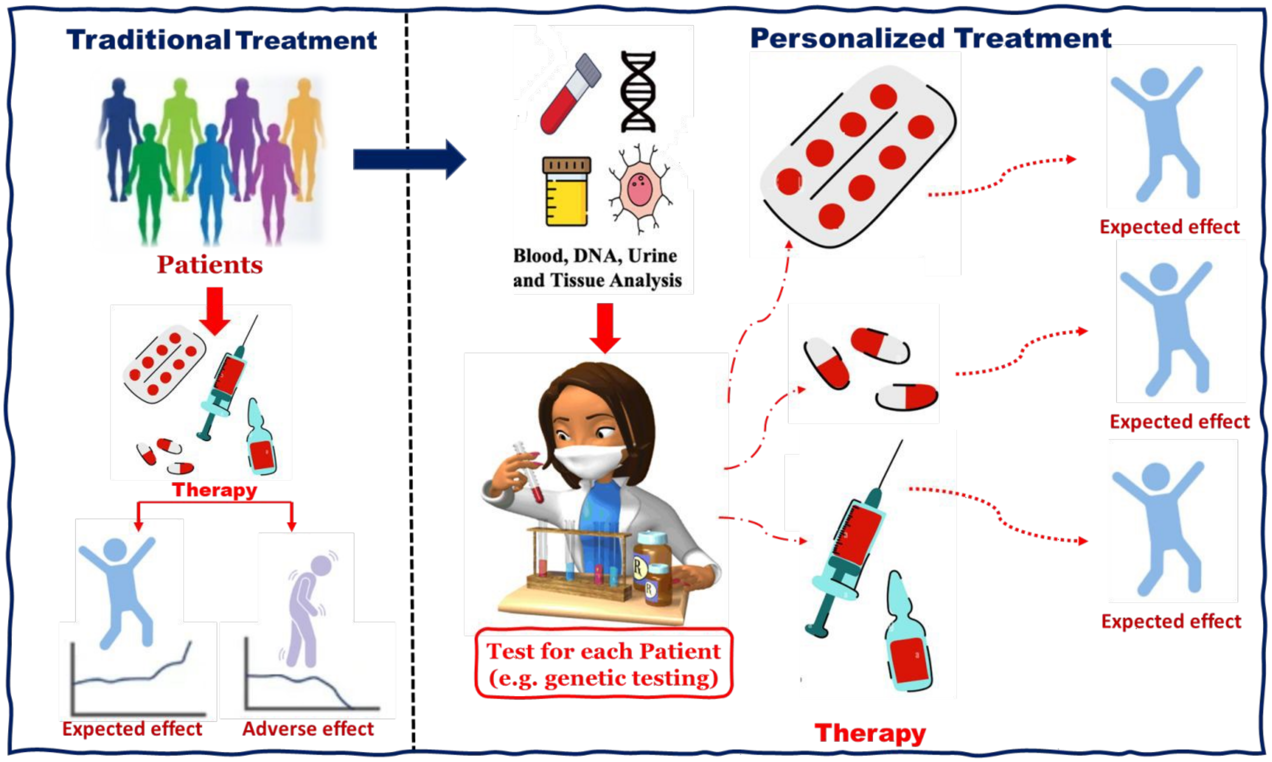

Fig.2 Traditional Treatment vs Personalized Treatment

7.2. Importance in chronic and rare diseases

There is a consensus among healthcare professionals that any medical treatment approach is patient-specific, but it is heterogeneous in disease and health state. Thus, the pharmacokinetics and pharmacodynamics are altered from person to person or may differ due to simultaneous medication for other diseases [120]. With respect to the varying pharmaceutical characteristics and the design of specific treatments for such rare diseases, considering the sporadic patient data creates a challenge in management and therapy compliance [121]. Additionally, most chronic diseases are accompanied by comorbid features, such as side effects that result from the interaction of multiple factors using combined therapeutic agents. Maximum medication response with minimal deterioration of the health state needs to be addressed to improve the patient's quality of life [122]. From pilot studies using cancer treatment to gene-targeted clinical trials, researchers have started to focus on personalized therapeutic regimens according to their recent findings and relevant databases. The present status of genetic and non-genetic factors of the disease needs to be discussed from the initial disease prediction towards the treatment scenario and its prognosis [123]. Precision medicine research is presently restricted

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to patients who are in good health, extensive medical technology, excellent public healthcare, and efficient data management systems, i.e., health smart devices, big data technology, and data-based models mostly used in treatment personalization [124]. Such growth is also heavily influenced by accelerated progress seeking pharmaceutical treatments for peptic ulcers, the eradication of H. pylori naturally, and the treatment of antibiotics for chronic hepatitis and some forms of cancer. More extensive pathologies, including cancer, chronic pancreatitis, inflammatory bowel disease, and hepatic cryoglobulinemia targeting the pancreas, stomach, intestines, liver, and other organs with the same success have recently emerged in gastric and liver drug delivery systems with fewer chemotherapeutic drugs [125]. As a result, treatment personalization also necessitates the ability to develop drug delivery systems targeting these areas. With novel vaccine and drug delivery, nanoparticles, nano emulsions, and their combination kits can address both rare and chronic pathologies, and the design of smart devices is urgently required.

8. AI Tools for Personalization

8.1. Genomics data analysis

Currently, recent technological advancements have launched the new field of "genomic medicine" and its focus on the influence of genetic differences on the development and progression of human diseases [126]. There is growing evidence to substantiate those genetic differences exist among patients in their response to drugs and their susceptibility to drug-induced toxicity. Pharmacogenomics, a branch of personalized medicine, identifies patient profiles that subject them to drug responses, thereby optimizing drug therapy, with competencies for clinical decision-making and improvements in drug safety and outcomes. In addition, treatment suggestions based on patients' genetic characterizations are necessary to solve the issues of adverse drug reactions and the lack of pharmaceutical efficacy [127]. The valuable information from whole genomes can be stored by diverse high-throughput functional genomics platforms employed for the comprehension of the function of genes. These potentially curative strategies are only showing substantial clinical success with the development of genome-sequencing methods, resulting in a wealth of protein variants, new therapy targets, and some therapies for rare Mendelian diseases that do not have other effective treatment options [128]. This

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requires the adoption of personalized care and the efficient delivery of safe, genome-edited cells to patients.

8.2. Patient stratification using AI algorithms

Highly heterogeneous disease biology is a problem that may not be resolved by targeting individual biomarkers. A growing trend in the clinical management of cancer patients is reclassifying patients into groups of similar prognosis and treatment efficacy, and more optimal therapeutic use of medicine[129]. Tumor stratification is subsetting cancer patients based upon the heterogeneity of cellular and molecular characteristics into clinically actionable population homogeneity. Although biomarkers such as estrogen or HER2 expression in breast cancer, activity of tyrosine kinase inhibitors in non-small cell lung cancer, and mutation testing before anti-EGFR treatment in colorectal cancer have demonstrated both clinical relevance and cost-effectiveness, additional biomarkers could predict if a particular drug is likely to have superior efficacy or disease-modulating activity in patients with a predefined genetic, proteomic, or metabolomic signature [130] [131].

A patient first arriving in the clinic has the potential to be corrected and immediately steered to the cluster with the best projected outcome using advanced predictive algorithms [132]. This can be achieved by attempting to learn from populations of pre-labeled patients by machines. Modeling patient behavior and the course of the disease can result in predictive models that can group patients in specific clusters, calling them strata, for which specific treatment decisions can be recommended. Although enabling this may still be a dream for healthcare regulators, AI has just finished entering the clinic [133]. AI has also been used to identify patient groupings for colorectal cancer, endocrine therapy in breast cancer, and drug effectiveness in systemic sclerosis.

To refine the potential benefits of using AI models for treatment guidance, clinical care must gradually become more personalized. This new treatment approach that has gained much attention in recent years is personalized medicine, also known as precision medicine [134]. In contrast to the one-size-fits-all treatment in decades past or patients classified by the stage of a disease, clinicians and researchers now integrate clinical, molecular, and patient readiness data to predict individual risk factors and to optimize treatment options [135]. The patient clinical pathway, diagnostic testing, patient qualification for participation in a clinical trial, treatment

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intervention, and support after treatment are tailored and more focused on the individual. In particular, the immune system of patients is the centerpiece of personalized medicine, and no two patients have the same immune profile at the same moment [136]. Such personalized treatment plans can be designed uniquely by integrating a patient's own molecular makeup, aggregates of molecular data, and AI technology [137].

8.3. Development of tailored therapeutics

The development of personalized therapeutic agents capable of targeting features or mutations in an individual is an appealing form of individualized medication that may help optimize health care [138]. Inherent to this approach is the capability to produce tailored drugs on a patient-to-patient basis with the same level of production efficiency as currently experienced in the mass production of drugs [139]. Advanced manufacturing techniques, now including techniques for gene editing and printing at the nanoscale, are increasingly being used in the pharmaceutical sector, accelerating the development of tailored therapeutics [140]. Even the development of drugs tailored to a particular target population that can take advantage of economies of scale associated with large patient groups is advantageous.

The development of tailored therapeutics can also be enhanced using artificial intelligence. Of specific interest is the concept of using intelligent software algorithms to help find optimal molecular therapeutics and geometric arrangements that best achieve a desired biological effect. The use of intelligent algorithms for the development of potential drug candidates can help to optimize attributes required of a potential drug, aiming to minimize typical poor in vivo drug performance, and help select drug leads that are more likely to lead to genuine improvement in the targeted therapeutic outcome. Allocating a greater effort in identifying lead drug candidates that are smaller and more diverse in structure and mechanism, addressing the current popularity for repurposing existing drugs, offers several advantages. Small molecules and groups of molecules having properties other than those associated with traditional drugs, and which have lower known safety concerns may receive heightened interest while advancing understanding of the behavior of molecules to support future drug lead optimization[141] .

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9. AI-Enhanced Precision Therapies

9.1. Case Study: AI in Oncology

Artificial intelligence (AI) has contributed substantially in recent years to cancer resolution. Cancer is the leading cause of death in developed countries. However, advances in early detection and improvements in therapeutics contribute to decrease cancer mortality and increase the amount of cancer survivors. Evidence-based medicine, based on a patient-centric approach, is rapidly replacing experience-based medicine. AI could revolutionize medicine, being the key driver of the transformation of healthcare to precision and personalized medicine. In oncology, there are major barriers for AI implementation, such as biased data, lack of standardized collection, insufficient clinical validation, or outdated regulatory frameworks. Big data is extremely useful in the digitization of healthcare. Traditional software approaches are not suitable for the challenges imposed by digital healthcare. Automated algorithms can help to process complex data and extract meaningful patterns, changing treatment evaluations and patient classifications. AI and 'machine learning' (ML) have achieved several important medical advances. In oncology, the question is 'How will AI improve the outcomes of patients with cancer?'. Major advances in technology have produced large-scale, multidimensional data for cancer research. Cancers are now understood as multifactorial diseases requiring unique treatment and management. New cancer diagnoses are focused on complex methods such as measurement of molecular features to match individuals to targeted treatment plans. Analysis and sharing of clinical data have become paramount as our knowledge of cancer heterogeneity grows[142]. The application of AI algorithms has the potential to transform health and healthcare delivery. Common applications of AI in healthcare include identifying conditions, risk factors, and patterns, which can support clinical decision making and improve treatment outcomes. The complexity of oncological diseases presents an opportunity for AI to impact oncology-related problems. However, few AI tools have had a significant impact in oncology. The goal of this study is to present an AI-based solution tool for oncology problems validated at a medical institution in Spain [143].

9.1.1. Impact on Treatment Personalization

Emerging AI techniques have shown promises in various aspects such as predicting genes related to drug side effect in an interactions network and similarly categorizing drugs

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based on structure or compound similarities that would help identifying some compounds that can intervene with the effect of drugs and thus serve as candidates for new generation drugs. From treatment strategy perspective, AI would have the capability to locate titleable genes from the whole genome at patient level to increase mutations predicted reliably and determine the patient cohort for a given treatment. With respect to treatment types, AI tools could assist in establishing the predict treatments based on previous treatment outcomes from exploratory to mechanism guided treatment. Other potential applications of AI reasonable less related to the molecular level include predicting diabetes development based on multi-phenomena records and analyzing co-event logs to note the potential drug abuse patterns of an individual. AI offers highly cost-effective and efficient platforms on local data outreach. Given the treatment choice, it could filter the most exemplar patients and give complementary recommendation for upcoming visits probability distribution based on the prescription. Such systems suggest the therapeutic procedures to patients and thus help dispensing tailoring treatment.

AI is expected to alter the treatment type greatly from exploratory treatment to mechanism guided treatment with the enhancement of health record data completeness. With respect to exploratory treatment type, treatment recommendation engines pursue related patients' previous treatment outcomes in databases and thus assist finding a wider candidate treatment. Most recently proposed recommendation systems are not capable or unsuitable to consult again and to highlight the insight of memories. A desired recommendation system should be patient level aware based on the developed validation method and a sample system has been demonstrated to consider the treatment candidate set as the context with incorporated local patients history and treatment recommendation. AI empowered prediction tools could open a door to the treatment types and recommend the appealing patient's cohort who tolerate better targeted medicines via data mining on genotypic, epigenetic, lifestyle, social networks and interactions, and environmental heterogeneities on drug metabolism, reactivity and biological activity [144].

9.1.2. Outcomes and Effectiveness

Due to the clinical team facing complexity in treatment drug and dosage selection, AI intervention is to be assessed with respect to outcomes and effectiveness by focusing on precision medicine in precision pharmacology, predictive view for experimental trials and early

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diagnosis of chronic conditions. Pharmacogenomic data, clinically approved drugs and associated dosage levels and generic information have been structured and analyzed, where the role of AI for both structure and prediction aspects as far as the application in pharmacology are concerned is discussed. The possible predictions are highlighted, where accuracy is increased with the inclusion of more features from both pharmacogenomic data and chemical structure descriptors. With respect to a predictive view on drug trials, potential failures of drug trial with respect to toxicity are assessed by structured analysis of toxicity data, where AI assistance in assessing target proteins, protein-ligand docking, adoption of lead compound selection, early toxicity assessment in addition to drug efficacy, and prioritization of compounds for wet-lab studies are assessed based on in silico datasets corresponding to a series of databases followed globally for applying AI modeling in drug toxicity are focused. New strategies powered by AI in tackling wishes for early chronic disease monitor and treatment based on big-data processing and machine learning model generation and assessment from current early chronic condition datasets are explored.

AI assistance is paramount in better targeted therapy through pharmacogenomic analysis and predictive pharmacology. The number of public available pharmacogenomic data resources has been updated and merged with pharmacogenomic knowledge base of drug treatment and targets in a user-friendly way entitled as PGP "Pharmacogenomics Database and Platform". Analysis of potential of AI in precision pharmacology with respect to how to do the task, outcome prediction and feature prediction has been a highlight of AI assistive in breath-taking medicine treatment and the current limitations in accessibility of the application is discussed. Through a combination of ML and NLP approach, the noted drugs in the COVID-19 context and the associated potential target proteins have been identified based on a merged database of globally available attributes in drug repurposing [144 145]. Though AI is outstanding in drug repurposing according to the collected initial knowledge, AI is trouble-some in preserving important weights and interpretable in counterfactual instances

9.2. Case Study: AI in Cardiovascular Medicine

Precision medicine is an evolving healthcare trend that aims to deliver personalized treatment protocols to every patient, particularly in cardiovascular medicine. The traditional one-size-fits-all healthcare approach has focused on generalization: everyone individual with

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hypertension, isosorbide dinitrate and/or metoprolol are prescribed, while all coronary artery disease patients with hypertension are treated the same. Cardiovascular medicine has numerous branches; for example, a patient with hypertension not accompanied by atherosclerotic cardiovascular disease, congestive heart failure, or post-myocardial infarction will be treated differently primarily just based on the symptoms related to that particular branch. On the other hand, a young patient with two-vessel coronary artery disease who developed an acute myocardial infarction without prior history will have an entirely different management approach than a middle-aged man having three-vessel coronary artery disease with prior history. Therefore, this approach requires proper understanding and processing of large amounts of real-world patient data sampled over time. Precision cardiovascular medicine aims to identify and analyze the right intervention for the right set of patients at the right time staging involved with quantifiable outcome assessment, which is time-stamped and persisted in raw data format [146]. The analysis of the data performed by human physicians is limited in the volume of data, the number of features involved in analysis, and processing speed, which are time-consuming and error-prone. There is a scope of AI-based methods assisting human physicians in understanding and optimizing the assessment of large amounts of patient data. Issues related to the input variable, extracting features, processing models, and understanding predicted outcomes require implementation of several different AI paradigms. An alarming implication of it for the healthcare provider is that machine-learning and deep-learning based algorithms employing hundreds of thousands or even millions input parameters provide prediction scores that do not offer real understanding of the processed data. The black-box nature of these models and the complexity of the data yield biophysical and medical implausibility of the predicted outcomes, which raises the need of research on interpretable AI and underlying biophysical process of the prediction scores.

Recently, AI-based methods have been evolving in precision cardiovascular medicine, attempting to improve patient care by analyzing patient data over time with quantifiable outcome assessments. As a result, the strategy involving a medical analysis of patient data with the involvement of AI means providing patient-centric data-assisted approach to human physicians. A systematic literature survey has been performed, by searching the most popular databases for the terms "precision medicine", "cardiovascular", and "AI" from January 1, 2010, up to July 10, 2023. Findings relevant to cardiovascular medicine, precision medicine, and patient care were

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considered. The focus was on AI implementations, biophysical models of predictions, and benefits of patient care improvement. The data sources reviewed suggest that there has been an increasing trend of research on precision medicine in the cardiovascular medicine domain in the last five years for AI implementation. The United States has reported the most research trends on precision medicine in cardiovascular medicine with a total of 16 papers, suggesting that these trends will continue to grow over time. The received papers have been classified into three broad categories, including cardiovascular branches, precision medicine branch, and AI algorithms.

9.2.1. Risk Assessment Models

Many ethical considerations surround the development and usage of Artificial Intelligence (AI) algorithms. The advancement of AI is creating a race for the development and deployment of AI algorithms primarily from the scientific and marketing viewpoints. However, it requires consideration of more than just technology, including ethics, governance, and regulation. Risk assessment algorithms are valuable and sought-after teaching tools in education at all levels, from Pre-Kindergarten to Universities worldwide. They are being increasingly developed by many organizations but without expected thought on what makes a robust and meaningful Assessment model.

In this study, the availability of better-trained and supervised AI systems due to growing data volume and quality is highlighted. State-of-the-art research efforts based on journal papers and patent analyses are also addressed in this regard. Therefore, potential data sources that allow doing something similar for developing a better risk assessment model, including healthcare organizations, online patient health data aggregation, and analysis, literature mining, text and image data, etc., are highlighted. Efforts made with academic collaboration to address some of these challenges such as the development of the AI guidelines and evaluation metrics are identified.

The potential threat to health and safety faced by a poorly implemented AI algorithm is stressed. The need for the establishment of an organization, similar to the FDA for AI systems, to ensure the validity, reliability, and ethical usage of the algorithm prior to any marketing and commercial use is also emphasized. The ever-increasing reliance on AI in health and society demands a wider recognition of the uniqueness of AI algorithms, addressing this challenge with prospective forethought rather than retrospective rectification. Machine Learning (ML) and

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Artificial Intelligence (AI) techniques are being increasingly incorporated into computer-aided diagnosis systems. These AI-based systems significantly improve the accuracy and reliability of breast cancer diagnosis and risk assessment. Many investigators have used their personal health data to identify breast cancer risk factors. Logistic regression, linear discriminant analysis, naive Bayes, and feed-forward neural network algorithms are utilized to predict the risk of breast cancer in 5 years' time [147].

9.2.2. Patient Management Strategies

Precision medicine has transformed the traditional practice of medicine from a symptom-driven approach to a design and procedure that studies a patient's genome to identify and treat ailments before symptoms appear. By enhancing and integrating diagnostic, prognostic, and predictive precision, quality is defined based on the analysis of metabolomics, genomics, and clinical data to drive its development and procedure. However, medical data analysis requires significant efforts from specialists in the respective administrative and statistical analyses geared toward the design of healthcare and research studies. Precision medicine relies on additional details from the healthcare environment to enrich medical conditions with genomic and metabolomic data. Subsequently, the integration leads to better prediction than the combined models. This is the functionality of intelligent and integrative approaches, models, tools, and technologies from which biomedical data quality, analysis, and mining engineering disciplines facilitate informatization and intelligent in-depth decision-making over heterogeneous biomedical data. A major limitation to the implementation of precision medicine is the amount of required analytic efforts where most of the efforts today are either manually-based or semi-automated. The requirements of interpretability of intelligence, consideration of heterogeneity, and balance between the size of method space for discoveries and conducted analyses of a method family exacerbated the hurdle [144].

The proper realization of precision medicine requires a progressive environment that facilitates the informatization of observational and experimental studies, so that the immense difficulties in analyzing big data will be taken care of by powerful tools and technologies. Towards the end, a self-contained biomedical health data cube consisting of healthcare plans, in-patients and out-patients records, clinical data, genomics, and metabolomics has been constructed and tools for data analysis have been developed. The self-contained cube allows

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unbiased heterogeneity detection and discovery as predefined users' criterion can be taken into account for data query. Data predictive analytics tasks are completed using local modeling-based and knowledge-driven method families that are characterized by a mode of explainable intelligence and ease of usage. Integration of predictions from data quality based human nature ensemble provides more robust and accurate results, thereby recovering the tedious effort required for proper decision-making [148].

9.3. Case Study: AI in Rare Diseases

AI technologies have made major strides in recent years, and expectations for future applications are huge. AI is expected to more efficiently detect early signs of rare diseases by analyzing different types of medical data and identifying patients whose symptoms resemble those of diagnosed rare diseases. AI is also expected to help test new candidates for drug development. This indicates that there is a massive need for systems capable of screening a huge number of compounds against many targets and predicting a huge space of pharmacological interactions.

There are excellent case studies on AI applications for drug treatment of rare diseases, one of them being protein misfolding diseases. There are also studies on the general detection of diseases by looking at images and texts. Some AI models generate molecular graphs and images of drugs with predicted affinity to targets based on previous knowledge. Some AI models are trained on sequences and 3D of targets to perform drug repurposing without any assumption regarding the functioning mechanism. There are AI models for mapping known drugs to new targets. Some algorithms merge existing data sources with novel data sources to build composite resources, yielding machine learning models with improved accuracy. It is now understood that well-defined learning tasks play an important role in machine learning model performance. Still, widely used self-supervised methods have no learning tasks to guide model learning.

There is only limited data available for a meaningful training of a model tasked with the identification of rare diseases. Some progress has been made in developing statistical methods validating the adequacy of a training dataset for a specific machine learning task. Detailed insights on state-of-the-art drug development approaches are given. Different AI methodologies are put in the context of selected rare diseases from the reviewed categories; state-of-the-art AI methodologies adaptable for rare disease targets. Significant new developments have taken place

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for a wide spectrum of rare disease treatment applications. The computational feasibility of AI treatments for ultra-rare diseases should also benefit a few more common rare diseases.

9.3.1. Tailored Treatment Approaches

The potential for precision medicine in clinical practice is vast. The following case studies demonstrate new technologies that leverage AI algorithms with the goal of tailoring treatment approaches. These technologies span pairs of drugs whose effectiveness differs from patient to patient, specific drug combinations that yield prolonged cancer remission in individuals with relapsed cancers, and a rare genetic disorder stemming from a single nucleotide variant. In each case, complementary technologies were required to detect patient-specific disease biology relevant for therapy selection. Together, these advances showcase the implementation of the principles of precision medicine with the goal of tailored treatment. There is great optimism regarding the positive impacts of AI algorithms on precision medicine.

Although precision oncology shows vast promise for many tumor types in an era of targeted agents, it has yet to deliver broadly in clinical practice. Camarillo's case involved a 43-year-old woman with stage IIIC ovarian cancer treated at multiple leading academic medical centers who failed all treatment options. Deep phenotyping in a patient-derived but genetically defined syngeneic organoid model identified sensitivity of rapidly progressive cancer to combination therapy with poly-ADP ribose polymerase and immune checkpoint blockade. In vivo, this combination yielded profound tumor regression, prolonged remission, and simultaneous immune-mediated rejection of disseminated metastases [149]. A wider appreciation of treatment paradigms across combinations of targeted therapies in breast, endometrial, pancreatic, and other cancers invigorate the development of de novo combinatorial therapies for these tumors.

Disease-specific platform technologies providing individualized precision medicine are also being combined with machine learning to discover previously unrecognized opportunities for drug repurposing. Camarillo's individual case study coupled targeted next-generation sequencing and droplet digital PCR of exometabolomics to inform lead compound selection for a novel, newly discovered WT1-p53 protein-protein targeting strategy for malignant pleural mesothelioma that was exploited for de novo combination therapy with Paclitaxel. A new ex

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vivo drug combination platform to guide treatment in patients with relapsed/refractory DLBCL is also under development [150].

9.3.2. Longitudinal Patient Data Utilization

With the advances of the Sensible City initiative and affordable mobile devices, some blue-collar workers are now equipped with smartphone-level internet-capable devices. The wide exposure to the internet in their work characteristics makes it possible to track the collective "social activity status" of the entire population in the city via their digital footprints. Commissioning a large-scale data survey using the back-end of their social media group enables the collection of the moving population's extensive survey responses and internet usage patterns. Capturing and analyzing epidemiological progress, individuals' response behaviour, and the operational conditions of large social gatherings will provide a far-reaching understanding of COVID-19 disparities inside and outside China [144]. The rather 'unitary' open policy across different counties has allowed capturing semi-experience-based intervention measures and responses to COVID-19 in the first place but made those more ambiguous in terms of digital usage gaps and social layering comparisons because of the divergence international media information landscape. With an adequate amount of invariant data and new AI-based analytical approaches, social disparities towards the spread and mitigation measures of COVID-19 would be quantized and mitigated. The design of an effective monitoring platform for machine learning-based public health monitoring based on heterogeneous data could be summarized as five steps including meta-data layer, visualized platform; adjustable alert mechanism; data-driven prediction approaches; decentralized & intuitive social media group-based intervention design.

Table 4. Examples demonstrating the various ways artificial intelligence is being used in industrial manufacturing

AI Application	Overview	Case Example	Ref
Synthesis Route Prediction	AI predicts optimal synthetic routes for APIs, examining chemical databases and literature to suggest efficient pathways	IBM's "Rxn for Chemistry" tool predicts chemical reaction pathways, used to streamline synthesis.	151

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Robotic Synthesis	Chemical synthesis is automated using AI-driven robotics, facilitating high-throughput testing and expediting the drug discovery process.	The University of Glasgow's "Chemputer" automates the production of medicinal molecules.	152, 153
Drug Design	AI identifies druggable targets by forecasting the molecular characteristics and structures of possible drug candidates.	In just 18 months, Insilico Medicine used AI to create a new medication for idiopathic pulmonary fibrosis.	154, 155
Drug Discovery	CRSIP technology and AI algorithms make it possible to determine which genes, when removed, result in cancer medication resistance or sensitization.	To find new targets for developing better drugs, AstraZeneca applied AI to CRISPR gene-editing technology.	156
Compound Selection	To find potential drugs candidates based on characteristics like solubility, permeability, and toxicity, AI evaluates chemical databases.	Exscientia discovered a novel compound for the treatment of immunomodulatory and inflammatory disorders using artificial intelligence.	157
Process Optimization	By examining production line data to find inefficiencies and suggest fixes, artificial intelligence (AI) optimizes industrial operations.	To increase yield and decrease production time for their COVID-19 vaccine, Pfizer utilized artificial intelligence.	158, 159
Continuous Manufacturing and PAT Technology	From acquiring raw materials to packaging the finished product, AI-driven optimization improves several aspects of pharmaceutical production.	AI was used by pharmaceutical companies to increase efficiency in continuous manufacturing.	160
Medical imaging	By streamlining workflows, improving detection, and automating time-consuming operations, AI systems have been developed to assist radiologists.	AI algorithms are being used by Bayer to minimize burden and provide patients with quicker decision-making.	161
Digital Twin Technology	To mimic, track, and optimize processes in real-time without interfering with actual production, artificial intelligence (AI) builds a digital twin, or virtual version, of the manufacturing process.	Johnson & Johnson increased productivity by simulating and optimizing their production processes using digital twins.	162
Predictive Maintenance	Artificial intelligence (AI) models evaluate sensor data from equipment to forecast when maintenance is required, preventing unplanned malfunctions and efficiently scheduling maintenance tasks.	Pfizer decreased maintenance expenses and downtime in its manufacturing facilities by implementing AI for predictive maintenance.	46
Supply Chain Optimization	By forecasting demand, controlling inventory, and streamlining logistics using performance data and market trends, artificial intelligence (AI) improves the pharmaceutical supply chain.	Novartis used artificial intelligence (AI) to handle supply chain logistics, which improved inventory control and cut expenses.	163

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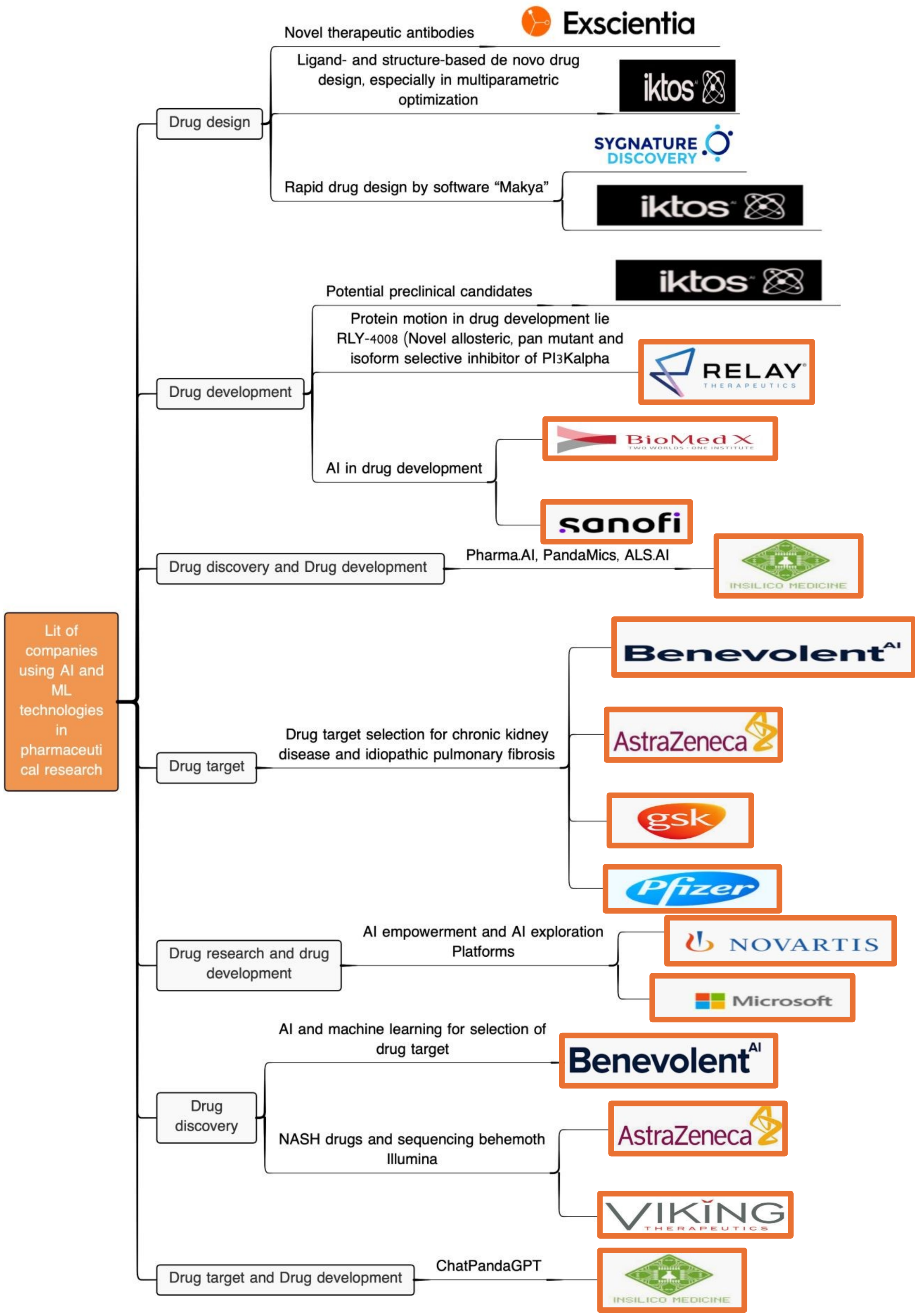

Fig. 3 List of companies using AI and ML technologies in pharmaceutical research

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10. Synergistic Role of AI in Smart Drug Delivery and Personalized Medicine

10.1. Combining drug delivery systems with real-time data from AI models

One of the major limitations of current drug delivery systems is the inability to receive feedback on their effectiveness over time. This could be due to varied responses in drug activity, disease changes, and individual responses [164]. However, with advanced technologies in diagnostics and imaging techniques, it is possible to monitor the drug delivery process and receive feedback on the drug's effectiveness in real time. Incorporating response data with AI models could have several positive implications, including but not limited to adjusting the drug dose, altering drug therapy, and modifying the delivery strategy for personalized drug delivery [165]. All these possibilities call for a more patient-centric and precision medicine-based approach. At the same time, AI models usually require very large amounts of data to achieve successful results, whereas data acquisition in this field, especially through the examination of clinical and preclinical entities for personalized medicine, is a challenging activity [166]. Combining drug formulations with AI algorithms is a promising strategy toward combating these issues. Indeed, tailor-designed drug delivery systems that can both respond to external signals and collect relevant data with built-in sensors are considered a proactive way to enable personalized therapy strategies. By analyzing collected information through machine learning algorithms, the response of the drug delivery system can be predicted for various scenarios. Such designed systems will significantly expedite and optimize health care and enable personalized drug therapy for chronic diseases, especially in cases with different patient response rates or different disease phases [167].

10.2. Patient monitoring and adaptive treatment plans

Patient health can be constantly monitored through wireless connected devices. Patient monitoring is already a key application of smart wearable sensors and microfluidic devices integrated into garments [168]. Advanced wearable development and artificial intelligence allow the introduction of context awareness based on the patient's environment and lifestyle, and personalized models for each patient for predictive association [169]. The industry is quickly applying this technology to injectable medical devices. Even if some of these advanced sensors and body systems have not yet been integrated into market products, several companies are testing wearable microfluidics products. These liquids are properly combined with the drug in

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the microfluidics process [170]. Other companies are developing artificial pancreas systems that can monitor plasma glucose concentrations. In this way, they aim to help the patient optimize their own pancreatic production of insulin. Such artificial intelligence systems are just the beginning of what individual patient health monitoring and diagnostic tests have to offer.

The consequence is that, soon, if a patient's wearable detects the symptoms of a health problem, a pre-trained algorithm will personalize the patient's precise medication at a specific dose. The health of the patient can be safely and automatically monitored outside of professional clinical environments and the patient's drug delivery management [171]. The patient's compliant medication may significantly decrease, and the algorithms will adapt the therapeutic plan to the current condition of the patient. This medication may minimize diabetes and cancer effects in some cases through natural extracts or can reduce chronic drug administration side effects [172]. Individual-specific real-time predictive monitoring is the next phase of smart connected drug delivery enabled by the integration of microfluidics into drug delivery devices. In this context, artificial intelligence connected with individual monitoring is processing the information gathered [173]. The aim is to make such decisions and advise the medication to the patient so that their health condition can be maintained at the best possible level.

10.3. Addressing pharmacokinetic and pharmacodynamic variability

High pharmacokinetic and pharmacodynamic variability between individuals is an important reason why patients need different doses and treatment regimens to achieve optimal therapeutic outcomes. However, the fixed dose commonly used in the clinic does not consider the variability between individuals [174]. The variability in drug concentrations in the body is determined by changes in pharmacokinetic parameters, such as reduced drug metabolism and reduced renal clearance. The current approach to addressing pharmacokinetic variability is not patient specific. Clinicians consider the patient's weight and BMI, as well as disease status and comorbidities, to adjust the dosage per protocol or based on effective medication [175]. Although the patient's genetic background can indeed be used to roughly predict the pharmacokinetic parameters of certain drugs, pharmacokinetic modeling and simulation technology can better predict the pharmacokinetics of drugs in patients, but it requires future blood concentration data [176 177].

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In summary, pharmacokinetic variability is the leading cause of improper treatment. However, various factors and covariates are not currently considered in dosing regimens. As a result, limited consideration is given to the different doses and dosing schedules needed for individuals to achieve the desired therapeutic effect [178]. Since the genetic background of the patient can reveal many pharmacokinetic-pharmacodynamic relationships, it would be possible to develop a model to predict the pharmacokinetics of a target drug in vivo through the patient's DNA, and then deliver the drug in a personalized manner [179]. Such an approach might also help to identify patients prone to adverse effects before undergoing therapy, allowing the dosage of the drug to be more customized for their use based on real-time pharmacokinetic information [180]. In addition, personalized monitoring information is also important to determine the biomarkers that best reflect the work of the drug and the patient's eligibility for medications [181].

11. Challenges and Limitations

By using AI to analyze patient databases, we are training algorithms on the data produced in these smart systems. This data holds every detail of the patient, diagnosis, co-morbidities, drug treatment, and its effects, as well as other personal details [182]. While the development of AI is crucial to the improvement of medicines, we must also ensure that we maintain patient privacy [183]. Anonymization is not enough, as training datasets using state-of-the-art models can lead to accuracy improvements in rendering data 'de-identified.' Personalization achieved by advanced data analytics techniques also requires the sharing of patient data and sometimes patient tissue at the sample level to implement the algorithm in clinical practice. Maintaining patient privacy during the lifetime of the field will require a fine balance to be struck between maintaining the power required for the AI to work effectively and anonymity [184]. This field is a current area of active concern.

The data needed to develop and use innovative drug delivery systems is rich and a perfect resource for data mining. The information will be used by a patient and by a future patient through machine-learning algorithms [185]. Overcoming patient health as an object in use on a smart drug delivery system raises data privacy and security issues and ethical concerns related to informed consent, data ownership, fiduciary responsibility, patient transparency, data security and integrity, intellectual property, and societal and individual rights among others [186]. The ethical considerations as well as innovation in materials and integration are important to bear in

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mind when developing personalized medical systems over smart drug delivery system platforms [187].

11.1. Regulatory and ethical challenges

The development of AI components in biomedical algorithms not only encounters these technical issues but also other challenges from both regulatory and ethical perspectives. One of the biggest regulatory challenges to AI algorithm development concerns clinical validation [188]. To obtain marketing approval or clearance from regulatory bodies, medical technology developers need to undertake empirical validation studies across a range of different environments and real-world users to demonstrate the safety and effectiveness of the technology [189]. The incorporation of AI into regulated medical technologies introduces an additional layer of complexity to the validation process, both from a technical and logistical standpoint [190]. A resulting regulatory challenge is how to properly account for the unique issues that arise from an AI system that learns over time from a range of different real-world sources of data [191] [192].

Developing ethical AI-based medical systems also presents many other contemporary bioethical issues, including accountability for AI's behavior and decisions; transparency to disclose the machine learning process and algorithm; preventing unfairness in the sense of harmful unintended bias; explainability and interpretability of an AI-based system's decisions; and reliability and stability in terms of unassertiveness or error [193]. The precision of algorithms in complex environments is of particular concern. Complications arising from misunderstandings of how machine learning tools work may affect the required knowledge of the tools, resulting in concerns relating to privacy, autonomy, and whether these tools unjustifiably challenge autonomy [194]. The intricate ways in which AI-related bioethics and self-governance, even autonomy in relation to people with changing goals and values, adds to the depth of complexity regarding the design of and reliance on AI tools such as drug delivery systems.

11.2. Risk of using AI in drug delivery and personalized medicine

Artificial intelligence (AI) is revolutionizing precision medicine and drug delivery systems. It offers immense potential to personalize immune responses, predict drug delivery kinetics, enhance pharmacological systems, and develop therapies for cancer and neurological disorders. By supporting drug design, chemical synthesis, biological evaluations, and decision-

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making in drug discovery, AI is an invaluable resource [195]. The advantages of AI include predicting drug-likeness, exploring vast chemical libraries, and identifying synergistic drug combinations. It also aids in understanding treatments for rare diseases and facilitates drug repurposing. AI excels at extracting relevant biomarkers, improving data accuracy in epigenomics and genomics, and predicting protein-DNA interactions, which enhance future clinical trial designs [196]. AI systems filter out data noise to prioritize compounds likely to succeed therapeutically, while safety models update toxicological databases, ensuring reliable information throughout drug development. Therefore, integrating AI into healthcare marks a transformative period, promising advancements in treatment precision and efficacy.

The domain of artificial intelligence in healthcare faces numerous challenges requiring careful consideration. A major issue is the lack of extensive, well-annotated cancer datasets, significantly undermining machine learning effectiveness [197]. The rise in false-positive melanoma detection rates, which can increase ten-fold compared to clinical diagnoses, highlights the urgent need for thorough validation [198]. As AI applications in health technology assessments grow, they outpace available data, raising important questions about potential consequences. Data privacy and security are critical concerns that demand careful attention [199]. The inherent trade-offs in sensitivity analysis complicate this balance between innovation and risk. Smart systems' reliance on algorithmic decision-making makes them vulnerable to security breaches, which could have serious repercussions. The risk of producing erroneous outcomes also calls for strong oversight mechanisms. Ignoring new relational dynamics can lead to a loss of knowledge, while overlooked side effects from flawed algorithms can intensify existing vulnerabilities. The lack of a human touch in AI-driven healthcare solutions raises significant issues, especially considering cultural differences in understanding mental health. Furthermore, algorithmic bias poses a threat by potentially perpetuating and exacerbating current inequalities in healthcare[200]. Therefore, addressing these multifaceted challenges requires a focused and proactive approach.

11.2.1. Data Privacy and Security Risks

The integration of artificial intelligence within the realm of healthcare revolves around the utilization of highly sensitive, primary personal data. The myriad of data privacy and security risks associated with the deployment of AI in personalized medicine and pharmaceutical delivery is substantial. Notably, the risks pertaining to data privacy encompass the potential for the re-

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identification of personal information that was intended to remain anonymized, alongside the peril of unjust discrimination stemming from the analysis and processing of such personal data [201]. Furthermore, the acquisition of personal data may precipitate its over-mining by data aggregators, thereby jeopardizing both patient rights and the competitive edge of enterprises engaged in AI-driven solutions.

Entities (data operators) tasked with the processing of personal data—defined as any information that can be linked to an identifiable individual-bear the responsibility for such processing. The General Data Protection Regulation (GDPR) endorses a principle of privacy by design and by default, mandating data operators to safeguard against unlawful processing, as well as accidental loss, destruction, or damage, while ensuring the availability and accessibility of data. Most principles established for the management of conventional personal data extend their applicability to data categorized under AI [202].

To accurately assess the risk associated with the processing of personal data in the context of AI, existing risk assessment tools tailored for personal data must be enhanced through the incorporation of novel methodologies that address the unique characteristics inherent to AI systems. Given the lucrative prospects associated with AI, the extensive collection of personal data is further amplified by intense competition among data operators striving to acquire more personal information [203]. Consequently, the processing of personal data not only introduces the risk of re-identification when an individual is acknowledged but also the danger of unfair discrimination, as it facilitates the discernment of particular individual attributes-both protected and unprotected in terms of discrimination.

11.2.2. Patient Data Protection

The concept of "digital sovereignty" has become crucial in discussions about governance, society, and technology, particularly due to extensive data collection. Managing digital resources involves significant ethical and philosophical implications that affect contemporary life. The debate focuses on data ownership, highlighting issues of privacy, autonomy, and individual rights [204]. The interaction among states, corporations, and digital platforms has created a scenario where personal data is commodified, often neglecting the tenets of consent and agency. Understanding the principles governing data collection, storage, and use is essential, especially given advances in AI and machine learning. Recent developments stress the need for strong

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frameworks to protect rights and promote transparency and accountability in digital environments [205]. Ethical concerns about data usage are heightened by pervasive surveillance, raising issues about personal freedoms and the potential for misuse of sensitive information. Data-driven decision-making impacts society broadly, affecting collective behaviours and exposing algorithmic biases and systemic inequalities that threaten fair resource distribution. Stakeholders must engage in discussions to define ethical data practices, prioritizing fairness, inclusivity, and human dignity. The conversation around digital sovereignty transcends technical challenges, embodying a societal necessity for re-evaluating data ethics . As we step into a more interconnected future, the focus on protecting individual rights and cultivating a responsible digital culture is vital for our collective progress.

11.2.3. Cybersecurity Threats

The evolution of artificial intelligence (AI) and machine learning (ML) in the past two decades has driven significant changes, especially in personalized healthcare and the pharmaceutical industry. This technological progress brings ethical challenges. AI models can produce unpredictable outcomes that reveal vulnerabilities, leading to complex, undesirable consequences. Creating AI/ML systems that avoid ethical issues is a substantial challenge, still largely unresolved. The rapid development of these models risks unintended repercussions that could spiral out of control, raising existential concerns about AI functioning against human welfare [206].

In pharmaceuticals, automated ML systems can process vast datasets to develop new medications rapidly. This efficiency, while promising potential cures for diseases like cancer, poses risks, such as the emergence of superbugs and the possibility of malicious entities deliberately releasing pathogens. Although no current pharmaceutical consortium is nearing this fast-paced research speed, such risks necessitate proactive measures to prevent dystopian outcomes. Additionally, as AI integration into daily life deepens, questions arise about ethical considerations in AI recommendations. Even though AI can suggest choices based on various values, it fails to provide data-driven solutions to ethical dilemmas, highlighting an ongoing complexity.

The increasing presence of AI systems may distort human perceptions of value, encouraging unhealthy attitudes and potentially promoting violent or unethical behavior.

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Moreover, AI capable of generating harmful code poses threats to users by exploiting their devices or networks. Advanced models can create realistic synthetic data, enabling malicious actors to produce convincing imagery or text with minimal coding skills. Such capabilities can expose security vulnerabilities and aid hackers, complicating the AI landscape. Deep learning models trained on code repositories may devise sophisticated exploits, further enhancing the challenges faced in AI governance and security [207].

12. Future Directions

12.1. Advancements in AI algorithms for better predictions

Artificial intelligence (AI) has increasingly enabled the development of intelligent systems and has been incorporated with a high degree of reliability across interdisciplinary fields in public health studies [208]. In commonly adopted research models, various AI algorithms have been demonstrated to be significantly effective [209]. AI models can be trained, optimized, validated, and used on different scales and have been shown to be superior at capturing non-linear trends, analyzing vast amounts of complex data, and performing disease or drug compound predictions in big data. Different AI algorithms inherently contain specific principles or are suitable for diverse applications. The motivation for this work is that many AI algorithms could be better used but are possibly underemployed. Generally, AI algorithms, from traditional statistical and mathematical modeling methods to recently trending deep learning methods, have been widely and effectively implemented in various drug discovery or development predictive analyses or trials [210]. Different AI algorithms contain distinct requirements and internal algorithms, and they are configured differently. The most used AI algorithms suitable for predictive analyses include random forest, support vector machine, convolutional neural network, and deep learning. When these methods are suitably configured, they can quickly present high performance. Understanding the operational principles, strengths, and limitations of the different AI algorithms is helpful for interdisciplinary professionals to execute a topic-sensitive design for the reserved models [72]. The AI algorithms can be better employed in terms of improved prediction results and reduced time-consuming or numerically aiming experimental designs.

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12.2. Potential of wearable technologies in real-time data integration

Several wearable tools and sensors have been designed to monitor numerous body-specific parameters in real-time. Personalized medicine can be greatly enhanced by wearable technologies integrated into smart drug delivery systems [211]. Wearable devices collect and convey real-time data of biomarkers and physiological indicators to the doctor continually [212]. These gadgets can provide real-time alerts, possess tiny form factors, are easy to operate and fix, and provide contact-free monitoring of the patient. The attendant sensors are capable of transducing data of the biochemical, electrical, or mechanical type. Being light in weight, these add a high level of comfort and do not skew the data obtained. A broad range of body-specific parameters can be directly monitored through the wearable technology, i.e., heart rate, pH, body temperature, blood pressure, movement, etc. Many diseases can be identified early on with the help of these types of devices [213]. These can be as diverse as managing self-health in fitness enthusiasts, chronic disease management, COVID-19 detection, or heart health and syncope monitoring. Since wearable gadget technology is cost-free, the opportunities for driving imaginations are limitless [214]. Certain clothing can have integrated skin sensors.

12.3. Collaborative frameworks between AI researchers and clinicians

There is no simple answer to how to ignite the implementation of AI frameworks in the clinic. A key challenge faced by many researchers is the realization that moving a proof-of-concept machine learning model into the clinical setting involves not just building a model, but the careful assessment of all single components that together form the system that will be validated in a clinical trial [215]. Therefore, suggest making machine learning algorithms more accessible to the clinical domain. By encouraging results to adhere to AI-driven protocols, domain-specific language requirements would regulate newly developed algorithms and delegate compliance to the AI agents [216]. The best approach to achieve this is the development of a standardized semantic knowledge framework to guide the development of future AI approaches and prioritize clinical needs. Similarly, for average clinicians to understand and critique AI-driven research, we need forward-thinking AI researchers to translate their work into language that is understandable without a degree in computer science. This reciprocal environment is extremely difficult to achieve, which is why we see interprofessional collaboration as the most important success factor for successful AI implementation in

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personalized medicine. Interprofessional collaboration requires frequent communication among AI researchers, domain-educated users, and decision-makers, as well as future AI developers and users of the system. Whether AI-driven management and triage, AI-driven therapeutics, or AI-driven augmented diagnostics are at stake, the role that AI will play within healthcare is growing [217]. Only through interprofessional collaboration can this growth be managed effectively.

12.4. Role of quantum computing in drug delivery and personalized medicine

Inspired by the large number of drugs approved daily by regulatory authorities around the world, scientists are engaged in customizing the necessary treatment that an individual patient may require and designing it precisely to reach the target site in a timely manner and quickly release the functional doses [218]. With the advancement of medical technology in recent years, continuous progress in the field of drug delivery has led to the conclusion that the introduction of quantum optimization of proteins (quantum optimization of proteins highlights the convergence of quantum mechanics and biochemistry. Using quantum methods to optimize protein structures is gaining traction, potentially reshaping our comprehension of molecular interactions as researchers explore quantum states' roles in protein folding and stability). and pharmacovigilance can pave the way to meet this challenge. With the introduction of quantum computing, novel ideas should be released immediately that can support the development of strategies to optimize prototype synthesis or facilitate combinatorial library selection [219]. Subsequently, we present a quantum computing model that optimizes the protein selection problem for open-loop drug delivery (The term "open-loop drug delivery" refers to administering therapeutic agents without real-time feedback or adjustments based on the patient's response) [220]. The concept of a quantum computer is a new one, and we seek to evaluate its effects in computer technology and the software industry. The relationship between the process of drug discovery and quantum computing is still in its infancy. Researchers, however, realize that the two areas are compatible and work to merge quantum computing and chemical problems [221]. The accelerated, disruptive technologies of quantum computing and quantum optimization begin to merge with strong interests in the future drug discovery market. The benefits that quantum computing can provide result from its nature as a real-time artificial intelligence algorithm [222].

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It provides real-time information by analyzing one molecule at a time, so one can quickly intervene when the forecasts show undesired results, which is positive in the field of drugs [223].

13. Conclusion

AI has revolutionized smart drug delivery and personalized medicine by enabling better characterization of drugs, real-time monitoring, and accurate therapeutic interventions. The use of AI-based strategies helps in patient stratification, pharmacovigilance, and multimodal diagnostics with the objective of timely identification of potential problems and optimization of nanoparticle-based therapeutics. Real-time personalized point-of-care diagnostics and predictive models to personalize dosing accuracy, minimize adverse effects, and ensure treatment adherence will lead to better, safer delivery of drugs. The integration of AI with genomics, proteomics, and biomarkers has definitely set a foundation for personalized treatment protocols. However, the realization of the potential of digital health will call for international collaboration, policy support, and strategic investments. Inspired by past technological revolutions, digital health must be prioritized to ensure equitable access to precision medicine and proactive disease management. Future innovations in AI-driven healthcare include combining sensory-based health monitoring with AI, IoT, robotics, and advanced medical devices. This integration will make possible early disease detection, personalized digital therapeutics, and remote monitoring, ultimately saving hospital costs and the burden that chronic diseases inflict on society. Despite challenges that arise from the AI-driven nature of medical devices and digital therapeutics, attention to real-world applications rather than theoretical models must be paid. AI-driven medical technology must focus on real-time diagnostics, self-management systems, and adaptive interventions to enhance patient outcomes and revolutionize healthcare delivery. With AI, the future of healthcare is changing toward a proactive, personalized, and technologically integrated approach, marking the beginning of a digital health revolution aimed at improving global health and well-being.

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This article does not contain any original data. All data discussed and analyzed in this review are derived from previously published studies, which are appropriately cited within the manuscript.