NAVIGATING THE HORIZON: EXPLORING FUTURISTIC TRENDS IN PHARMACEUTICALS AND DRUG DELIVERY SYSTEMS

Abstract

The pharmaceutical sector has seen tremendous improvements in medication delivery technologies in recent years. These cutting-edge innovations, which range from tailored medicines to nanotechnology-based solutions, are transforming pharmaceutical administration and improving its efficacy. This chapter explores how innovations in personalized medicine, nanotechnology, and novel medication delivery methods are altering the precise treatment of disease. The emphasis is made on how innovation and focused interventions are reshaping the healthcare scene and creating a bright future. From ancient herbal medicines to contemporary drug development procedures, the story develops with the advancement of pharmaceutical science. The complexity of diseases, the rising cost of medication research, and the incorporation of cutting-edge technologies like AI-driven drug design, 3D printing, and nanotechnology are some of the elements driving this progression. Additionally, it examines how regulatory actions, rising technology, and the Industry 4.0 revolution have affected pharmaceutical modernization efforts. Biopharmaceuticals, mRNA vaccines, 3D printing, nanotechnology, AI-driven drug development, and smart drug delivery systems are among the upcoming trends that are being investigated. This thorough viewpoint offers insights into the changing pharmaceutical industry, as well as the opportunities and difficulties it poses. The present chapter explores pharmaceutical trends: evolving technology, advanced drug delivery, biopharmaceuticals, 3D printing,

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nanotechnology, AI in drug discovery, and smart delivery systems, providing insights into the future landscape and challenges.

Keywords: Artificial intelligence, Internet of Technology, 3D-printing, Monoclonal Antibodies

I. INTRODUCTION TO FUTURISTIC TRENDS IN PHARMA AND DRUG DELIVERY

Emphasizing the vital role of the pharmaceutical industry, this chapter explores groundbreaking trends in drug delivery systems. These advances, spanning personalized medicine to nanotechnology, are revolutionizing disease treatment with enhanced precision. The broadening array of drug delivery techniques, encompassing implants and gene-based therapies, holds the potential for elevated patient outcomes. The evolving healthcare panorama is characterized by innovation and targeted interventions, shaping a promising future.

1. **Evolution of Pharmaceutical Technology:** The pharmaceutical industry stands as a pivotal and swiftly advancing sector globally. With its role encompassing the creation and manufacturing of remedies addressing a spectrum of ailments, from everyday illnesses to life-threatening conditions, the industry's evolution has been remarkable. From its inception to the present day, the industry has consistently pushed the boundaries of innovation to enhance the entire drug development process, encompassing formulation, production, and delivery.

   Embedded within the pharmaceutical sciences, pharmaceutical technology pertains to the intricate domains of drug composition, formulation, preparation, manufacturing, and quality control for both custom-prepared and commercially produced medications. It encompasses the multifaceted processes that underpin the creation of pharmaceuticals, optimizing their effectiveness and safety. This facet of the industry harmonizes with the overarching goal of refining treatment methodologies, ensuring that the drugs developed offer maximum therapeutic value while minimizing potential risks(Pharmaceutical Technology Core Concepts - Czech Pharmaceutical Society, n.d.).The pharmaceutical industry, a rapidly evolving cornerstone of modern society, traces its roots to an age where the journey of drug discovery was influenced by the relentless pursuit of overcoming illnesses. People's keen observations and recognition of a plant's healing properties, often through trial and error, played a pivotal role in this process.These traditional methods, an interplay of ancient wisdom and practicality, formed the foundation upon which the industry now stands(Sumner, 2001).

   Addressing the discovery of aspirin as a historical example for early pharmaceutics, the story of the willow tree (*Salix* sp.) unfolds across the annals of time, etched in clay tablets and historical accounts(Wells, 2003). The narrative of aspirin's lineage extends back over 3500 years. In ancient times, willow bark's pain-relieving properties remained unknown to the Sumerians and Egyptians who employed it, with salicin, its active agent, forming the bedrock for aspirin's eventual discovery (Lévesque & Lafont, 2000; Desborough & Keeling, 2017; Montinari et al., 2019). Willow leaves were used to treat a variety of diseases in Assyrian records from the Sumerian era (3500-2000 BC). Similarly, the Babylonians used willow tree extracts to treat fever, discomfort, and inflammation. This botanical heritage continued, with the Greek physician Dioscorides advocating willow bark for inflammation reduction, a practice that merged plant properties with medical wisdom to illuminate an early instance of pharmaceutics, healthcare, and drug development (Chevallier, 1996; King, 1974; Burns &Fulder, 2002).

As centuries marched forward, the historical curtain rises on the 18th century, initiating the modern era of aspirin discovery. The story of aspirin, now one of the most widely used drugs worldwide, begins with its birth in 1897. The evidence of willow bark's analgesic use emerged in 1862 through artifacts that dated back to the 1500BC, one of them currently known as the Edwin Smith Surgical Papyrus and the other one called Ebers Papyrus, detailing ancient herbal remedies and the use of salix (willow) for pain relief(Bryan, 2021). Through the rise and fall of empires, willow bark's healing attributes persisted, endorsed by eminent figures like Hippocrates and Pliny the Elder(Lévesque &Lafont, 2000; Lichterman & Diarmuid, 2004; Desborough & Keeling, 2017; Montinari et al., 2019).The advancement of natural remedies gained momentum with the revelation of the fever-relieving properties of cinchona bark. Reverend Edward Stone, in 1763, investigated the use of willow bark, laying the foundation for its potential in treating fevers(Stone, 1763). The journey continued with pioneers such as Johann Buchner and Pierre-Joseph Leroux refining willow bark into crystalline forms, eventually leading to the isolation of salicylic acid. The journey culminated in 1897 when chemist Felix Hoffmann synthesized aspirin, a significant stride toward modern medicine(Lévesque &Lafont, 2000, Desborough & Keeling, 2017 and Montinari et al., 2019). This historical narrative bridges the past with the present, revealing the inception of pharmaceutical technology.

From these historical origins, the pharmaceutical industry emerged as an agent of transformation. Rooted in large-scale production of drugs, including organic chemicals and dyes, the industry's impetus gained traction post-World Wars. A pivotal shift in global perspective saw the recognition that technological progress could eclipse the devastation wrought by conflicts. The potential to heal and restore lives through innovative compounds became evident, spurring the establishment of enterprises dedicated to concocting remedies for injuries and diseases caused by pathogenic microorganisms.This fervent pursuit of improvement aligned with nations' aspirations to elevate their standing and enhance life expectancy. The quest for novel compounds designed to combat ailments became an emblem of progress. The historical thread woven through the discovery of aspirin and the evolution of pharmaceutical technology merges seamlessly with this narrative, forging a continuum of innovation that reverberates through the ages. The exploration of historical remedies and the evolution of modern pharmaceuticals converge to illuminate a tapestry of progress, fueled by the indomitable human drive to conquer challenges and elevate the well-being of societies worldwide (Malerba & Orsenigo, 2015). In this intriguing tapestry of history and innovation, the pharmaceutical industry emerges as an ever-evolving force, propelled by the legacy of the past and the inexorable drive to enhance human well-being.

2. **Need for Advancement in Pharmaceutical Technology:** The pharmaceutical industry has been an instrumental force in enhancing global well-being over the last several decades, contributing significantly to increased life expectancy and the stability of healthcare systems (IFPMA, 2022). As the industry continues to evolve, driven by a multitude of factors, its pivotal role in both healthcare and the global economy becomes increasingly evident. This dynamic evolution is underscored by the constant push for innovation and modernization, shaping a landscape characterized by groundbreaking technologies and novel approaches to drug development, manufacturing, and delivery.

One of the foremost drivers propelling the evolution of the pharmaceutical industry is the escalating complexity of diseases. The ever-deepening understanding of the molecular underpinnings of various ailments has empowered scientists to develop treatments with enhanced precision and efficacy. Personalized, targeted medications have emerged, diverging from the conventional approach (Schmidt et al., 2020).

The escalating costs associated with drug development further fuel the industry's transformation (IFPMA, 2022). With the price tag of bringing a new drug to market soaring into the billions, pharmaceutical companies are compelled to explore innovative avenues to mitigate expenses (Destro and Barolo, 2022). This financial pressure has catalyzed a quest for cost-reduction strategies throughout the drug development lifecycle, from research and discovery to manufacturing and distribution. The industry's financial landscape has also led to a shift in focus towards diversification and the pursuit of new revenue streams.

The integration of advanced technologies defines the modernization of the pharmaceutical industry. Innovations like AI-driven drug design and 3D printing streamline drug discovery and delivery. Deep learning expedites drug repurposing, using patterns to uncover molecular relationships, enhancing efficiency (Nag et al., 2022; Pan et al., 2022). 3D printing aids personalized medicine by creating drugs for specific patients, particularly in hospital settings (Wang et al., 2023). Nanotechnology transforms drug delivery, with nanoparticles targeting cancer cells, minimizing side effects. Despite challenges, nanoparticles hold promise for cancer treatment (Tracey et al., 2021; Waheed et al., 2022). In summary, these innovations reshape pharmaceuticals, delivering precise treatments for enhanced patient outcomes.

Undoubtedly, COVID-19 spotlighted the pharmaceutical industry's agility and innovation. Swift vaccine and treatment development showcased its adaptability under duress. This crisis spurred remote marketing, while research focus shifted to COVID-19 treatments. Long-term impacts include approval delays for non-COVID drugs and supply chain disruptions, fostering self-sufficiency. Economic downturn might slow growth, with ethical concerns emerging in increased clinical research. Altered consumption habits due to hygiene practices and telemedicine's rise are transforming healthcare delivery. This response demonstrates the industry's resilience and adaptability, heralding shifts from production to healthcare in response to global challenges (Ayati et al., 2020).

The Industry 4.0 revolution has emerged as a revolutionary force in this setting. This change in thinking entails the digitization and automation of processes, aiming for autonomous decision-making through algorithmic operations. Industry 4.0 not only streamlines operations and reduces costs but also aligns with regulatory objectives for improved quality assurance and faster time-to-market (Destro & Barolo, 2022).

Moreover, the pharmaceutical sector is influenced by an intricate interplay of regulatory initiatives. The foundation for modernisation efforts is laid by current good manufacturing practices (cGMPs), process analytical technology (PAT), and quality by design (QbD). As the industry adopts these frameworks, emerging technologies like continuous processing, closed-loop control, and mathematical modeling are poised to redefine pharmaceutical development and manufacturing (Destro and Barolo, 2022).

This chapter delves into future trends in pharmaceuticals and drug delivery. It examines the evolution of pharmaceutical technology and the need for advanced drug delivery methods. The text explores biopharmaceuticals like monoclonal antibodies and mRNA vaccines, as well as 3D printing for personalized medicine. Nanotechnology's impact on drug delivery, AI and machine learning in drug discovery, as well as intelligent drug delivery systems are discussed. The chapter concludes with insights into the future landscape and challenges of drug delivery, offering a comprehensive view of the evolving pharmaceutical field.

II. BIOPHARMACEUTICALS AND NOVEL THERAPEUTIC MODALITIES

Biopharmaceuticals are a class of pharmaceutical goods that include any biological product created by or from living organisms utilizing recombinant DNA technology, such as therapeutic proteins, vaccines, and cellular and gene therapies. More than 300 Biopharmaceutical drugs have entered the market in the last 40 years. According to a recent analysis on the utilization of the many accelerated medication development and review programs provided by the US Food and medication Administration (FDA) between 2008 and 2021, 97 of 139 (70%) approved biologic drugs used one or more expedited programs (Schaefer et al, 2023). These products' biological origins can offer novel mechanisms of action for treating a range of indications (such as cancers, autoimmune diseases, genetic disorders, or infectious diseases), and the therapeutic recombinant proteins that are currently commercially available range from hormones and growth factors to interferons and enzymes (Szkodny et al, 2022).

1. **Monoclonal Antibodies and their Applications:** A novel family of drugs known as monoclonal antibodies (mAbs) binds extremely precise targets or receptors.The development of mAbs with novel biological properties, such as humanized, chimeric, or murine, as well as the widely utilized hydrodoma method, represents a significant medical advancement and has the potential to greatly improve disease management.

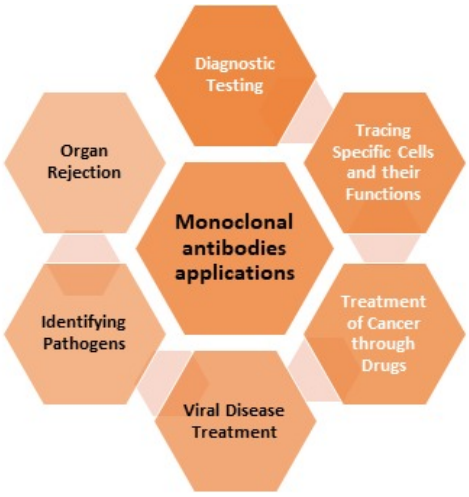

Figure 1: Applications of Monoclonal Antibodies (Ansar & Ghosh, 2013; Mahmuda et al, 2017)

A popular methodology for creating therapeutic antibodies from nonhuman origins is the hybridoma technique. In this method, immortal myeloma cells are fused with B lymphocytes that have been isolated from mice who have received an antigen vaccination. Antigen-specific mAbs are produced by hybridoma cells, however fusion efficiency can be poor and nonhuman mAbs may have negative downstream effects (Mokhtary et al., 2022). Peter M. Bowers and colleagues developed a novel method for collecting and producing human antibodies by combining in vitro somatic hypermutation (SHM) and mammalian cell display. SHM is reliant on the B cell-specific enzyme activation-induced cytidine deaminase (AID), which can be produced as recombinant AID in non-B cells. This method allows for direct antibody selection and full-length, glycosylated IgG maturation. This technique has been used on lines of human B cell lymphoma (Chaudhuri et al., 2004).

For a variety of scientific and therapeutic applications, monoclonal antibodies that target carbohydrate chains (glycans) are essential. Glycans are crucial for cellular functions such as protein folding, adhesion, and signaling. Anti-glycan antibodies are necessary for identifying and comprehending their biological functions. For studying current anti-glycan mAbs and finding novel ones, glycan microarrays are useful tools. However, there is little unified data on the majority of anti-glycan mAbs. This problem is addressed by the Database of Anti-Glycan Reagents (DAGR) and GlycoEpitope, which offer details on current anti-glycan mAbs, including targets and sources. Anti-glycan mAbs that are more advanced, superior, and varied are still needed. The discipline would benefit greatly from a comprehensive, searchable database of anti-glycan mAb sequences (Gillmann et al., 2023).

Changes in the biomarkers of the MAB targets and subsequent processes support the effects of anti-amyloid MABs on the underlying neurobiological mechanisms of Alzheimer's Disease (AD). The FDA has approved two anti-amyloid monoclonal antibodies for the treatment of Alzheimer's disease (AD), lecanemab and aducanumab. These treatments are the first disease-modifying drugs to delay clinical deterioration by interfering with the illness's fundamental molecular processes. These ground-breaking medications can halt the development of severe cognitive impairment due to AD (Cummings et al., 2023).

2. **mRNA Vaccines and Gene-Based Therapies:** In order to alter a protein's expression or cause other recognizable changes, therapeutic genetic material is delivered to a target tissue during gene therapy. While germline or somatic cells can be employed for gene therapy, somatic cells have been the focus of the majority of studies and medication development.

mRNA vaccines have been developed for several disorders, such as infectious diseases and specific cancer vaccines. The COVID-19 vaccines developed by Pfizer-BioNTech and Moderna are two significant examples of how the COVID-19 pandemic has propelled research toward mRNA vaccines for infectious diseases. The FDA approved the first two SARS-CoV-2 mRNA vaccines in 2020. Both vaccines were developed as LNPs that encapsulated mRNA with ionizable lipids. Among the other mRNA vaccines for infectious diseases now being developed is an LNP-based vaccination based on influenza A and B viruses that encode hemagglutinin antigens. The goal of mRNA cancer

vaccines is to boost cellular immunity by targeting tumor antigens. The BNT112 and BNT113 vaccines, which are tailored to certain individual mutations, and the FixVac BNT111 vaccine, aimed at four melanoma TAAs, are two examples. For the treatment of different cancers, the safety, tolerability, and effectiveness of the BNT122 combination vaccination are currently being examined (Fayez et al., 2023).

As a result of advancements in cancer biology, over 40% of cancer patients may experience a better quality of life thanks to monoclonal antibodies that can treat a variety of tumors more quickly and affordably. This study is regarding CAR-T cell therapy, a cell gene therapy that employs a chimeric antigen receptor to make a monoclonal antibody, CAR. Patients' T cells are taken out and modified so that they will attach to the cancer cell antigen CD19 and kill it. Despite being FDA-approved, it is not very popular (Srirapu et al., 2023).

Due to its modular architecture, effectiveness, and adaptation to novel viruses, inhalable mRNA vaccines provide shelf-stable, long-lasting protection against respiratory diseases. To address specific translational issues in the lung formulation and delivery environment, Next-generation mRNA vaccine combinations will be developed to make use Polymer and lipid extracts, along with next-generation pulmonary prediction algorithms, were studied. The mucosal immune system and pulmonary epithelial tissues can directly be reached by aerosolized vaccinations, but the respiratory tract has Physical, chemical, and biological barriers that prohibit particles from moving. Extracts with a high molecular weight, are hydrophobic, and/or have a ring-stacking structure, whereas non-interactive coatings prevent aggregation. The efficiency of mRNA is increased and endosomal escape is facilitated by adjusting the particle's pKa values to the pH of the endosome. Predictive evaluation of innovative aerosol therapies will improve with the use of advanced multiscale and ALI models of pulmonary barriers (Roh et al., 2022).

Endogenous genes called miRNAs are essential for cell proliferation, differentiation, and survival. Disease onset and progression are strongly influenced by abnormal miRNA expression and function. The aging population may benefit from treatment for neurological illnesses due to gene therapy, an increasingly potent technology. AAV was used in ALS gene therapy study by Foust et al., which greatly slowed the course of the illness and increased survival time. Successful gene therapy research in preclinical models and clinical trials are now possible via improvements in vector design and delivery technologies that have made it easier to target the brain and spinal cord (Foust et al., 2013; Liu et al., 2022).

Due to its ease of use, low cost, and great efficiency, CRISPR/Cas9 has swiftly emerged as the preferred gene-editing method globally. consists of a Cas9 nuclease, which creates a double-stranded break (DSB), and a guide RNA (gRNA), which locates the loci of interest within the genome. gRNA sequence specificity affects the sensitivity and specificity of CRISPR/Cas9. New Cas9 variants and modified guide RNAs enhance on-target activity, minimize off-target effects, and provide long-lasting gene modification. In human cells, high-fidelity SpCas9 and hyper-accurate Cas9 have demonstrated effectiveness. Adeno-associated virus (AAV) vectors can be divided into two for larger biochemical loads. Dual AAV vectors have been shown to be successful in treating HemA in pre-clinical investigations. In order to integrate human FVIII into the albumin locus,

two vectors harbouring Staphylococcus pyogenes Cas 9 and guide RNA with human B-domain deleted FVIII were employed. This resulted in liver production of FVIII for at least 7 months without off-target effects or liver damage (Segurado et al., 2022).

III. NANOTECHNOLOGY REVOLUTIONIZING DRUG DELIVERY

1. **Drug Delivery Systems:** Drug Delivery Systems (DDSs) transport a substance (a drug) from the outside to the body's target area. Drug efficacy is decreased and its therapeutic effect on the condition it is intended to treat is diminished when drug accumulation occurs in non-target areas. The DDSs' ability to deliver medications into certain tissues and cells preferentially allows them to successfully treat ailments. DDSs are developed by taking into account:
    - **High Therapeutic Level:** range of a drugs concentration in blood that is effective and safe.
    - **Increasing the Bioavailability of the Drug:** Bioavailability is the percentage of drug that reaches the systemic circulation (or cardiovascular system) to allow the drug to travel through blood vessels and other barriers to reach its target site of action.
    - **Reducing the Side Effects:** The DDSs can be divided into two main types: conventional DDSs and novel DDSs or controlled DDSs.

2. **Conventional DDSs:** These are the traditional approaches used to deliver medications to the body. These methods are more frequently utilised when a drug's rapid absorption is the main objective and a speedy release of the drug is necessary. Simple oral, topical, inhalation, or injectable procedures are some of the traditional medication delivery modalities. These techniques have some drawbacks, including the inability to maintain a steady drug concentration over time. Multiple dosages given at regular intervals are one way to solve this issue. However, this appears to be improper as there is a possibility that the patient would overlook taking the prescribed dose at regular intervals.

3. **Novel DDSs:** According to Reza Rezaie et al., (2018) it is also referred to as controlled-release drug delivery, this method combines cutting-edge methods with novel dosage forms to improve medication potency, regulate drug release, increase safety, and specifically target a drug to a target tissue. Controlled release necessitates two qualities in the release kinetics: predictability and reproducibility.

Table 1: Advantages and Disadvantages of Controlled-Release Drug Delivery

Advantages	**Disadvantages**
(1) Increased medication bioavailability and duration of effect. (2) Reduced drug degradation and loss. (3) Reducing medication concentration variations in plasma. (4) Improved utilization	(1) The materials' potential toxicity. (2) Harmful degradation products. (3) High cost (4) Synthesis procedure.

NDDSs are divided into four categories including (1) rate-preprogrammed, (2) activation-modulated, (3) feedback-regulated, and (4) site-targeting DDSs.

- **Rate-Preprogrammed DDSs:** Modification of the system design that regulates the diffusion rate of drug molecules through the barrier medium around it affects the rate or speed of a drug release.
- **Activation-Modulated DDSs:** Some physical, chemical, or biological processes, as well as external energy, stimulate the drug's release. Therefore, by adjusting the application procedures or the amount of external energy, the kinetics of release can be altered. Modification of the system design that regulates the diffusion rate of drug molecules through the barrier medium around it affects the rate or speed of a drug release.
- **Feedback-Regulated DDSs:** In this type of DDS, sensors that monitor the concentration of specific biochemical substances are built into the DDS devices (feedback mechanisms), and the concentration of these biochemical agents controls how much medicine is released.
- **Site-Targeted DDSs:** delivers a specific amount of a therapeutic agent for an extended period of time to a targeted diseased area of the body.
  - Passive targeting: This mechanism occurs when macromolecules cling to the targeted tissues as a result of the heightened permeability and retention phenomena.
  - Active targeting: This mechanism occurs when particular interactions occur between the nanocarrier and target cell receptors.

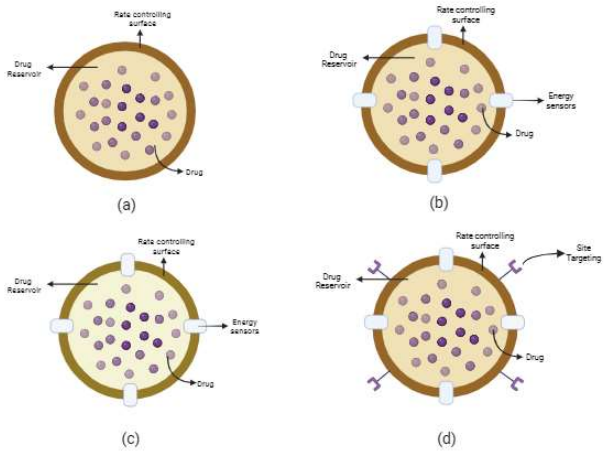

Figure 2: (a) Rate-preprogrammed DDS **(b)** Activation modulated DDS **(c)** Feedback-regulated DDS **(d)** Site-targeting DDS

4. **Routes of Drug Administration:** Route of Administration talks about the path taken by the drug to get into the body.

- **Oral Delivery:** This is the drug administration method that is most frequently utilized. With this approach, both systemic and local effects can be easily attained. Different drug concentrations can be found after each dose because this technique of delivery shows no control over the drug's release. Oral DDSs should consistently deliver a quantifiable and repeatable dose of a medicine to the target site over an

extended period of time. Tablets, capsules, syrups, and other products that are taken orally and pass through the digestive system are considered oral delivery.

- **Buccal Delivery:**Buccal mucosa lines the inner cheek, and buccal formulations are injected between the upper gingivae (gums) and cheek (also known as the buccal pouch) to treat both local and systemic illnesses. Buccal delivery techniques include mouthwashes, sprays, gums, bio-adhesive tablets, gels, and patches.

- **Rectal Delivery:**Suppositories are put inside the rectum and liquefy at body temperature in this system. This method of delivery is beneficial for comatose patients and youngsters who are vomiting. It is an efficient method since it avoids the first pass effect.

- **Parenteral Administration:** In this method the drugs are inserted into vascular tissues. This type of administration is preferred in case of emergencies when rapid absorption is required.

- **Topical Administration:** The application of medication to the surface of the skin or mucous membrane of the eye, ear, nose, mouth, vagina, etc. with the intent of limiting the pharmacological effect of the drug to the surface or within the layers of skin or mucous membrane is referred to as the topical route of drug administration. Topical medications are typically available in the form of creams, ointments, gels, lotions, sprays, powders, aerosols, liniments, and drops.

- **Inhalation:** Administration of drug within the respiratory tract by inhaling orally or nasally for local or systemic effect.

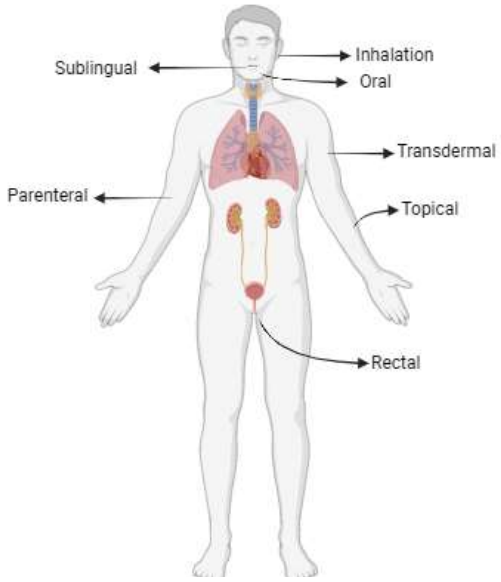

Figure 3: Routes of administration

5. **Drug Delivery Vehicles:** Several methods of packing medications so that they can transport safely throughout the body are represented by drug delivery vehicles. Various

drug delivery vehicles can help medications get exactly where they need to go, increasing drug targeting. Drug delivery vehicles' (DDVs') size, shape, surface chemistry, stiffness, and chemical composition all have an impact on delivery efficiency. The DDV's core is meant to be a repository for chemotherapeutics, DNA/RNA, or imaging agents. The outer component of DDVs, according to Poon et al. (2020), aids in avoiding innate and adaptive immune detection and is in charge of in vivo navigation.

- **Nanocarriers as Drug Delivery Vehicles:** Nanoparticle DDVs are resistant to the violent conditions of the circulatory environment, extending their halflives; they have high surfacetovolume ratios capable of providing a diverse array of multivalent ligand displays, allowing for enhanced immunestealth, targeting, cellular internalization, and delivery of their therapeutic payload; and they can be prepared from a wide range of inexpensive organic, inorganic, and biological materials used to encase them. Because nanoparticles are materials made at the atomic or molecular level, they are typically small spheres. As a result, they can move more easily in the human body than larger materials. Nanoparticles have distinct structural, chemical, mechanical, magnetic, electrical, and biological properties. Nanomedicines have gained popularity in recent years due to the fact that nanostructures can be used as delivery agents by encapsulating or attaching therapeutic pharmaceuticals and delivering them to target tissues with greater precision and controlled release. Nanostructures remain in the blood circulatory system for an extended period of time, allowing combined medications to be released at the prescribed dose. Because these structures are nanosized, they can enter the tissue system, allowing for easy drug uptake by cells, effective drug transport, and action at the intended spot. The utilization of an optimum nano-drug delivery system is mostly determined by the biophysical and biochemical properties of the targeted medications chosen for therapy. As mentioned by Vinothini & Rajan, (2019) the nanocarriers including nanoparticles, micelles, carbon-based materials, liposomes, niosomes, dendrimers, and other carriers are frequently used for DDSs.

Table 2: Types of Nanocarriers for drug delivery, their properties and representation

Nanocarrier	**Definition**	**Composition/ Structure**
Liposomes	Liposomes are small spherical artificial vesicles that contain at least one lipid bilayer.	Composed of phospholipids, especially **phosphatidylcholine, and cholesterol** Can also employ Ligands to detect diseased tissues
Micelle	Micelles are colloidal entities that are amphiphilic. Micelles are made up of molecules with two distinct water affinities.	Composed of ionic surfactants (cationic, anionic)

Polymeric Nanoparticles	Polymeric nanoparticles (NPs) are colloidal systems made from natural or synthetic polymers that can have particle sizes of up to 1000 nm.	**Natural Polymers:** Hyaluronic acid, Chitosan, Cellulose etc. **Synthetic Polymers:** Polyesters, PGA, PLA etc.
Dendrimer	Dendrimer is a synthetic polymer with a repeating chain structure that commonly forms spherical macromolecules.	Has three units: (1) centre of dendrimer or core, (2) repeated units like branches extended from the core, and (3) many functional groups located at the surface of the dendrimer
Niosomes	Niosomes are hydrated vesicular structures containing nonionic surfactants, phospholipids, or cholesterol that transport medicines to specific places.	Composed of: • Non-ionic Surfactants • Phospholipids
Inorganic Nanoparticles	Inorganic nanoparticles are nanoparticles composed of substances other than carbon.	Composed of non-carbon-based molecules, non-metal elements and forms of hydroxides or phosphate compounds.

- **Inorganic Nanoparticles for Drug Delivery:** Several organic nanoparticles derived from polymers, liposomes, and micelles have been researched and successfully created. Some of its intrinsic disadvantages include limited chemical stability, drug release rates that are suboptimal for the specific application, the likelihood of microbiological contamination, and the negative effects of the organic solvents used for particle formation. Because of their high cellular absorption capacity, non-immunogenic reaction, and low toxicity, inorganic nanoparticles have gotten a lot of attention as medication or gene delivery carriers. They have markedly different physical, chemical, and biological properties than their bulk counterparts. Shape and size have been shown to have a considerable influence on the electromagnetic, optical, and catalytic properties of noble-metal nanoparticles such as gold, silver, and platinum.

- **Nonporous Silica Nanoparticles (NSNs):** These are one of the most important types of silica nanoparticles, the silanol groups present on the surface of these nanoparticles can be functionalized easily using amine or carboxyl groups. As a result, NSNs with positive, negative or zwitterionic charges can be prepared. These nanoparticles can be used in hydrophobic drug delivery systems and delivery of gene and small molecules. There are two general strategies for incorporating drugs into/onto silica matrix in nonporous silica nanoparticles: (a) encapsulation and (b) covalence bond. In covalence attachment, drugs are covalently bonded with siloxane groups through degradable ester bonds. However, the encapsulation strategy involves the covalence attachment of drugs with the silica matrix through co-condensation with tetraethyl orthosilicate (TEOS) via the Stöber method (The Stöber process is a chemical process used to prepare silica (SiO_2) particles of controllable and uniform size for applications in materials science). The release of encapsulated drugs can be accomplished by decreasing the pH, since the decrease in pH can lead to decomposition of silica nanoplatform.

- **Mesoporous Silica Nanoparticles (MSNs):** Mesoporous silica nanoparticles are promising candidates as novel drug delivery system. Large internal surface area, extremely high pore capacity controllable morphologies (size and shape), biocompatibility, ease of synthesis, and ease of surface functionalization are among their significant properties in various nanomedicine applications, particularly as nanocarriers for drug delivery systems. In these nanoparticles the encapsulated drugs can be allowed to release by using the GSH-triggered stimulation method. In this strategy disulfide linkages between capping agents and the surface silanol groups of MSNs are reduced by intracellular GSH, this leads to removal of capping agents thereby releasing the loaded drugs.

- **Gold Nanoparticles:** Colloidal gold nanomaterials with different size and shape (e.g., nanorods, nanocages, nano cubes) are good candidates as nanocarriers for biomedicine and drug delivery. The ease of their preparation, their stability, low cytotoxicity, and high extinction coefficient of light from visible to NIR regions have introduced them as important candidates in cancer drug and nanocarrier development. (Mattoussi& Rotello, 2013)

- **Zinc Oxide Nanoparticles:** In recent years, Zinc Oxide nanoparticles (ZnONPs) emerged as an excellent candidate in the field of optical, electrical, food packaging and particularly in biomedical research. ZnONPs show cancer cell specific toxicity via the pH-dependent (low pH) dissolution into Zn^{2+} ions, which generate reactive oxygen species and induce cytotoxicity in cancer cells. Similar to elemental zinc, ZnONPs are also biocompatible towards normal mammalian cells due to its low dissolution rate, but causes oxidative stress and subsequent cell damage within cancer cells due to its rapid dissolution into Zn^{2+} ions at slightly acidic pH, thereby ZnONPs show pH-responsive cytotoxicity.

IV. ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING IN DRUG DISCOVERY

The multiple-stage process of developing new drugs uses a lot of resources. It might require up to two decades to get a drug on the market (Grechishnikova, 2021).Through the development of computing and analysis approaches utilising AI and big data algorithms, the limits in the conventional discovery of drugs area brought on by the scale and complexity of biomedical data can be computationally formulated and solved (Lee et al, 2022).Due to their capacity to automatically extract features from the input data and their potential to capture nonlinear input-output correlations, deep learning techniques, which are artificial neural networks that have multiple hidden processing layers, have recently drawn new interest. Algorithms for deep learning have several advantages over more conventional machine learning methods, which rely on hand-crafted molecular descriptors (Jimenez-Luna et al, 2021). Artificial Intelligence can identify hit and lead compounds, as well as accelerate therapeutic target validation and structural design optimization (Paul et al., 2021).

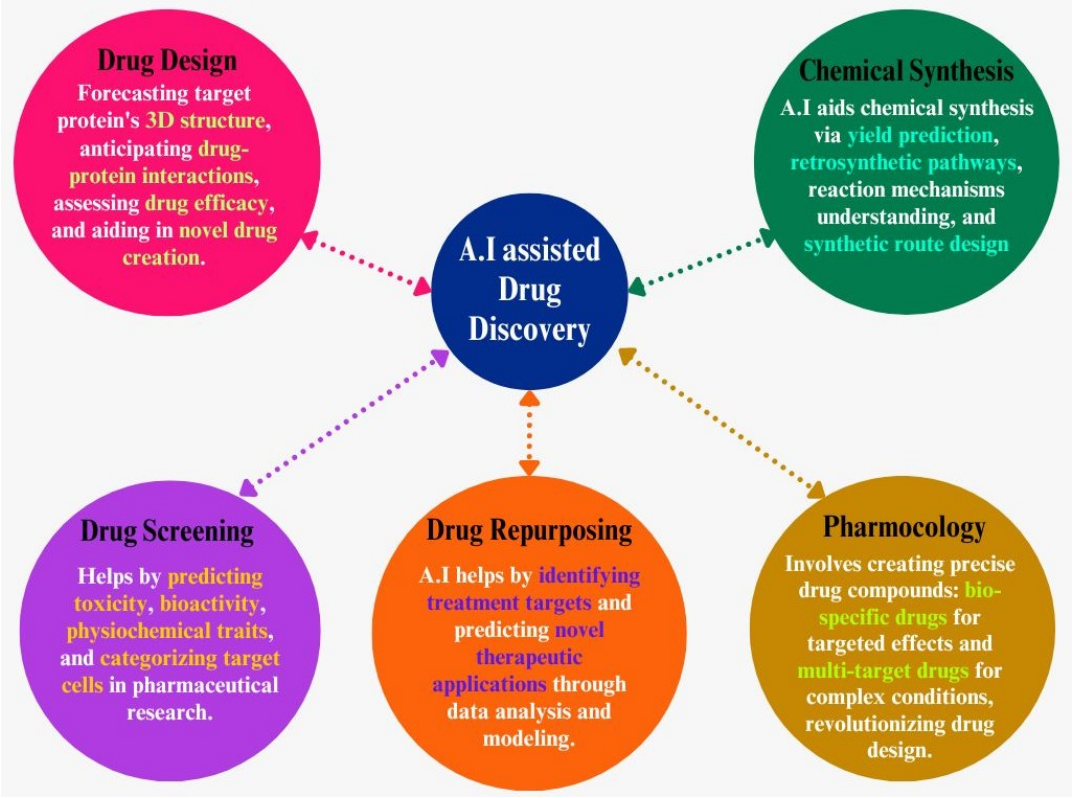

Figure 4: Artificial Intelligence Assisted Drug Discovery (Paul et al., 2021)

1. **Predictive Modelling for Drug Development:** As mentioned earlier, artificial intelligence has abilities to identify hit and lead compounds quickly reducing the overall time needed for drug discovery (Paul et al., 2021; Lee et al., 2022).

    - **Structure Based QSAR/QSPR Modelling:** In the more than 50 years since its start, QSAR/QSPR modelling has advanced significantly. The effectiveness of these computational models in predicting metabolism or biological activity and pharmacokinetic characteristics, such as absorption, distribution, metabolism,

elimination, and toxicology (ADMET), is conclusive proof of their influence on drug discovery. The so-called molecular descriptors are often used to translate structural characteristics of molecules (such as pharmacophore distribution, physicochemical properties, and functional groups) into machine-readable numbers for ligand-based QSAR/QSPR modelling. Hand-crafted molecular descriptors cover a wide range and attempt to describe many different facets of the underlying molecular structure. In order to deal with more complicated and possibly nonlinear interactions among the structure of a substance and its physicochemical/biological properties, QSAR/QSPR approaches have generally moved away from the use of simpler models, such as linear regression and k-nearest neighbours, and towards more broadly applicable machine learning techniques, such as support vector machines (SVM) and gradient boosting methods (GBM), often at the expense of interpretability (Jimenez-Luna et al., 2021).

- **Denovo Drug Development:** Due to the cardinality of the chemical domain of drug-like molecules, which is estimated to range in the order of 10^{60}-10^{100}, de novo design, the generation of novel molecular entities with desired pharmacological properties from scratch, can be considered one of the most difficult computerised tasks in drug discovery. De novo molecule production is challenged by combinatorial explosion since there are so many potential atomic kinds and molecular topologies to explore. Ligand-based methodologies can be broken down into two main groups: (i) rule-based approaches, which use a set of construction rules for assembling molecules from a set of 'building blocks' (such as reagents or molecular fragments), and (ii) rule-free approaches, which do not use explicit construction rules. The Topliss strategy for the sequential production of analogues of an active lead chemical to maximise potency is one of the precursors of modern rule-based de novo design. Modern methods for optimisation are based on using a predetermined set of molecular transformations, such as matching molecular pairs or rules-of-thumb for changing functional groups and molecular frameworks. Building block assembly and ligand production are explicitly included in synthesis rules in synthesis-oriented techniques. For example, these methods can be used to create artificially available libraries like BI CLAIM and CHIPMUNK. Since the late 1990s, hybrid approaches have been created to guide the synthesis of novel substances by both maximising their similarity to recognised bioactive ligands and the design's potential for chemical synthesis. Examples of these hybrid approaches are TOPAS, DOGS, and DINGOS. The majority of deep learning-based de novo design studies to date have emphasised ligand-based strategies. Targeting orphan receptors and previously unstudied macromolecules can be accomplished through the promising complementary research area of structure-based generative design (Jimenez-Luna et al., 2021). The majority of recurrent neural network (RNN)-based deep learning models for molecule production use this technology. RNN is frequently utilised to model sequence data. Utilising data from earlier steps is the primary characteristic of RNNs that enables them to function with sequential data. RNN can make connections between far-flung sequence pieces visible. RNNs are unfortunately plagued by the issue of disappearing gradients, which severely restricts their capacity to deal with lengthy sequences. This problem is somewhat resolved by gated recurrent and long short-term memory units. Recurrent neural networks based on short-term and long-term memory have recently been employed in various works for the development of de novo molecules. Simplified

Molecular-Input Line-Entry (SMILES) string input is used by them. The models are forced to produce targeted molecule libraries with the appropriate activity towards the same target when fine-tuning on a smaller dataset with compounds that are known to be active against biological targets. In the reinforcement learning paradigm, the agent (generator in the de novo drug generation issue) performs a step to maximise reward (function computed after SMILES string completion). This step involves choosing the next character during new SMILES string generation (Grechishnikova, 2021).

V. SMART DRUG DELIVERY SYSTEMS AND IOT INTEGRATION

Systemic side effects are frequently associated with conventional drug delivery systems (DDSs), which can be attributed to their unpredictable drug release properties and non-specific bio-distribution. Advanced controlled DDSs have been created to achieve the release of payloads at the target places in a spatially controlled manner, overcoming these constraints. Smart-controlled DDSs have an advantage over traditional DDSs in that they can reduce dosing frequency while preserving the concentration of drugs in the targeted organs and tissues for a longer duration. In this way, the controlled DDSs offer insightful information and intriguing characteristics for lowering drug concentration fluctuations, lowering medication toxicities, and enhancing therapeutic efficacy. These drug delivery systems can be developed which can be responsive to various stimuli like pH, Enzyme, Temperature, Redox, Light, Magnetic, ultra sound, and various other stimuli (Liu et.al., 2016). The "internet of things," or IoT, is a network of physical technologies that communicate data using built-in sensors, software, and connection. It enables automated communication and task completion between devices. By increasing productivity, automating operations, and offering cutting-edge data analysis, IoT can change entire sectors. Through smart devices, remote control, and in-the-moment data analysis, IoT-based medicine delivery systems maximise effectiveness, accuracy, and safety (Raikar et.al., 2023). Smart drug delivery systems have a great deal of potential to increase medication adherence and ease the strain of complicated regimens. By utilising their connectivity and smooth data exchange capabilities, IoT-based systems provide special benefits for smart medicine administration (Liu et al., 2016; Raikar et.al., 2023).

1. **Implantable Devices for Controlled Drug Release:** The drug rate of release is influenced by the physicochemical characteristics of the drug, such as solubility, particle size, and molecular weight, as well as the features of the polymeric coating, such as polymer configuration, molecular weight, and coating thickness (Pons-Faudoa et al., 2019). Devices or materials for regulating a chemical's release time, rate, or both are referred to as "controlled release" (Langer, 1990). A range of controlled drug delivery systems have been created during the past few years as a result of the expanding capabilities of conventional drug administration. Amongst these, MEMS-based drug delivery devices, micropumps and osmotic pumps, are used. These devices were created using various manufacturing processes and are used in a variety of administration methods (Sutradhar & Sumi, 2016).

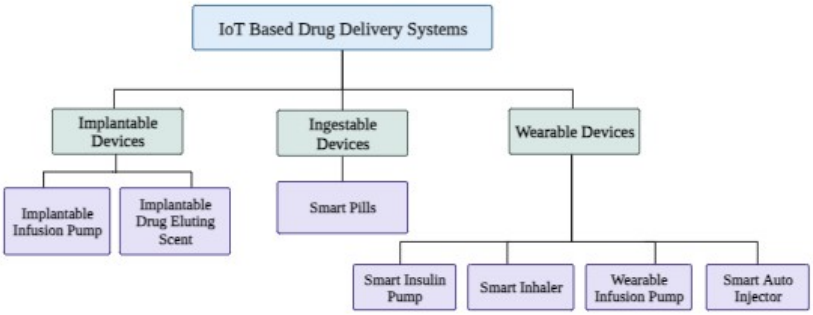

Figure 5: Classification of IoT-Based Drug delivery devices (Sutradhar & Sumi, 2016)

2. **Reservoir-Based Polymer Systems:** Passive implants known as reservoir-based polymer systems is one of the most popular controlled medication delivery methods to date. In these types of systems, a drug core is enclosed by a polymer film, and the polymer's properties (such as its composition and molecular weight), the coating's thickness, and the physicochemical characteristics of the drug, such as solubility, drug particle size, and molecular weight, all influence how quickly the drug is released (Pons-Faudoa et al., 2019; Yang & Pierstorff, 2012). Reservoir-based systems are best suited for either of the following two uses:
   - A localised medication that is administered over a medium to long period of time to a particular area (e.g., an organ, body cavity, etc).
   - A medication depot used in systemic long-term delivery.
   - Reservoir-based polymer systems are categorized into injectable, implants and hydrogels.

3. **Pumps:**

   - **Osmotic Pumps:** In order to give drugs to animals, Rose and Nelson created osmotic pumps in the 1950s. Since then, a variety of designs have been used in clinical settings to treat human ailments. Drug delivery systems called implantable osmotic pumps were created for long-term, sustained administration of treatments spanning months or years. After the pump is implanted, the mechanism for osmotic pump-driven medication release takes place. A high concentration of osmolytes (salts), or the osmotic engine, propels an osmotic flow of interstitial fluid over the semipermeable membrane. A force is applied to the piston by the inward H_2O flow, which raises the hydrostatic pressure in the osmotic reservoir. When a piston is pushed in the direction of a drug reservoir, the drug solution is injected in an amount equal to the volume that was previously displaced (Pons-Faudoa et al., 2019).

   - **Infusion Pumps:** Pharmaceutical preparations can be administered through a catheter inserted under the skin by wearable infusion pumps. They provide continuous medication throughout the day and are inconspicuous, portable devices that are set up to provide exact doses at predetermined intervals. By preventing disruption to the infusion site, wearable infusion pumps minimise the risk of infection while providing easy and mobile drug delivery. For individualised care, wearable infusion pumps

provide exact dosing and can modify medication based on current glucose levels (Raikar et al, 2023).

- **Peristaltic Pumps:** Peristaltic pumps are made up of rotary solenoid-driven systems that are powered by an external source, usually a battery. Peristaltic systems, like infusion pump systems, are loaded through a silicone rubber septum and can be used for years depending on how long the battery-powered device lasts. The advantage of this type of technology is that an external remote control system may regulate how quickly medications are supplied. However, due to their expensive cost, these devices have not yet been widely deployed (Kumar & Pillai, 2018).

4. **Microfabricated Systems:** Electromechanical technologies provide unique approaches to medication release in relation to precise dosing. Microelectromechanical systems (Eg: Microchips) and nanoelectromechanical systems (Nanochannel membranes) are terms used to refer to microscopic and nanoscopic devices containing features in the microscale and nanoscale array, respectively.When these implants are reduced in size, the forces that influence drug release vary in relation to the reduction in area and volume; adhesion and surface tension, for example, have a more significant impact on molecules, which is useful for controlled drug delivery (Pons-Faudoa et al., 2019).

5. **IoT-Enabled Monitoring of Patient Response:** IoT sensors continuously monitor drug delivery parameters, patient responses, and ambient conditions with real-time monitoring and data analytics, enabling quick intervention and improved treatment procedures (Liu et al., 2016). Health care providers may remotely track patient progress owing to remote access and connectivity, which makes them especially useful for telemedicine and the management of chronic diseases. Mobile apps, wearables, and interactive interfaces that encourage increased patient engagement enable patients to actively participate in their therapy, which improves self-management as well as treatment results (Saunders et al., 2019).

IoT-based drug delivery systems are gaining popularity in healthcare due to their potential to enhance medicine distribution precision, effectiveness, and efficiency. These systems utilize various algorithms for smart medication delivery, enabling data analysis, informed decisions, and treatment optimization. Closed-loop control algorithms, such as in closed-loop insulin delivery for diabetes, monitor real-time sensor data to determine proper dosage or delivery rates. Pharmacokinetic and pharmacodynamic algorithms leverage mathematical models to optimize dosing and predict medication responses based on factors like absorption, distribution, metabolism, and excretion. Machine learning algorithms analyze large datasets to identify patterns guiding dose decisions and improving treatment outcomes. These algorithms enable real-time notifications, adaptive dose adjustments, and dosing suggestions, enhancing drug delivery system efficiency, security, and treatment effectiveness (Hassanzadeh et al., 2019; Raikar et al., 2023).

VI. CHALLENGES AND FUTURE SCOPE

Drug carrier systems play a crucial role in controlled or targeted drug delivery. Associating established therapeutic compounds with nano-carriers holds the potential to revolutionize drug efficacy assessment and enhance our capacity to address various human ailments. The utilization of nanocarriers as conduits for drug delivery presents a blend of challenges and promising future prospects within the medical realm. Obstacles encompass concerns about biocompatibility and safety, the demand for large-scale manufacturing, maintaining stability and shelf life, achieving precise targeting, surmounting biological barriers, and ensuring efficient clearance and biodistribution. The assurance of biocompatibility and safety remains of paramount importance, while efficient and economically viable methods for mass production are required. The accuracy of targeting is a pivotal determinant for the success of therapeutic interventions, necessitating the circumvention of physiological barriers such as the intricate blood-brain barrier. In the sphere of potential, significant advancements await, including the realm of precision medicine, tailored therapeutic approaches, synergistic combination therapies, the delivery of genetic material like genes and RNA, innovative imaging and diagnostic capabilities, modulation of the immune system, mitigation of unwanted side effects, and the advancement of regenerative medicine. Nanocarriers offer the unique ability to carry diverse therapeutic agents, enabling the pursuit of multifaceted treatments addressing multiple facets of a condition simultaneously. Additionally, their aptitude to serve as imaging agents for diagnostic purposes, interact with the immune system to bolster responses, and reduce systemic side effects associated with conventional drug administration, underlines their vast potential for reshaping medical practices.

Monoclonal antibodies (mAbs), and mRNA gene-based therapy have revolutionized medicine by providing tailored treatments for various illnesses. However, challenges like cost, accessibility, immunogenicity, and delivery techniques remain. Advances in genomics and proteomics will enable personalized medicine, combination therapies, and cancer immunotherapy. Despite these challenges, the future of these medicines is promising, with extended therapeutic applications, vaccine innovation, genetic disease cures, combination therapies, neurological illnesses, and reduced global health disparities. Addressing these issues is crucial for their full potential and proper incorporation into clinical practice.

With breakthroughs in QSAR modeling, de novo molecular design, and synthesis planning, AI applications are gaining traction in drug discovery and design. However, the efficacy of these strategies in generating and synthesizing superior medication candidates has yet to be proven. Deep learning systems, such as graph neural networks and SMILES-based recurrent neural networks, can be used to a broader set of chemical entities and modeling tasks, allowing for more efficient data usage via multitasking and online learning. Although conformation-aware deep learning is still in its infancy, considerable improvement in drug discovery and related fields such as quantum mechanics and material science is expected. In de novo drug design, rule-based and rule-free approaches have been supplemented, with hybrid methods providing a pragmatic answer. Gene expression, conformation space, and ligand binding site information, among other sources of information, will continue to drive innovation in automated synthesis planning and reaction prediction. To develop and test these strategies, more interdisciplinary research is required.

Significant progress has been achieved in the evolution of implantable microchip technology, starting from its initial inception to the present day. It is evident that in the near future, implantable microchips hold the potential to supplant conventional drug delivery systems that are currently prevalent. As a promising avenue, substantial advancements are required to enhance the capabilities of these implantable microchip devices. These improvements encompass various aspects such as biocompatibility, precise dimensions and contours, heightened patient adherence for administration, and enhanced efficiency in delivering drugs within the surrounding bodily fluids. However, the journey towards realizing these advanced implantable microchips is not without its challenges. The forthcoming development of these microchips faces the task of scaling up manufacturing processes while maintaining quality and efficiency. Furthermore, there lies a necessity to refine the existing implantable microchips, transforming them into multifunctional devices capable of fulfilling diverse biological and therapeutic requirements during their operational period.

The rapid proliferation of IoT medical devices presents challenges due to their battery reliance, necessitating effective power management for device longevity. Merging big data with IoT healthcare systems can provide valuable insights by organizing patient data into comprehensive datasets. IoT-enabled health monitoring systems have revolutionized healthcare by providing real-time disease monitoring, accurate error detection, fewer doctor visits, and reduced patient expenses. However, future research should address potential challenges such as data security, privacy concerns, and compatibility issues. The collection of private health data by healthcare sensors and devices introduces risks of unauthorized access, breaching patient confidentiality. Data security issues include physical protection, secure communication routing, transparent data handling, and resource-efficient practices. Compatibility issues arise from the varied data collection needs of different devices. Addressing societal impacts, ethical considerations, service quality, and refining technological attributes is also crucial for its effective evaluation and implementation.

VII. CONCLUSION

This chapter provides a comprehensive exploration of futuristic endeavors in the realm of pharmaceuticals and DDSs. It delves into the evolutionary journey of pharmaceutical technology, highlighting the imperative for advanced drug delivery methodologies. The realm of biopharmaceuticals, exemplified by groundbreaking innovations such as monoclonal antibodies and mRNA vaccines, offering insights into their potential for treating a range of ailments. Noteworthy breakthroughs like antiamyloidmAbs, now approved for Alzheimer's treatment, demonstrate the industry's commitment to addressing intricate disease processes. The aftermath of the COVID-19 pandemic on the advancements in pharmaceutics is evident in the surge of genetic therapies like CAR-T cell therapy, as well as the development of inhalable mRNA vaccines, demonstrating the field's resilience in times of crisis. Nanotechnology emerges as a pivotal player, revolutionizing drug delivery through nanocarriers that overcome conventional challenges, paving the way for more personalized and efficacious treatments. Incorporation of AI and machine learning into the discovery process of drugs underscores their transformative capabilities in handling complex biomedical data and accelerating hit/lead identification. In the sphere of DDSs, the advent of smart technologies takes center stage, offering advanced mechanisms for precise drug release and real-time monitoring. From implantable devices to IoT-integrated solutions, these innovations not only enhance treatment efficacy but also streamline patient care. Challenges

and opportunities abound, from refining nanocarrier drug systems to ensuring data security in IoT devices. The landscape of pharmaceuticals is further enriched by the revolutionary potentials of monoclonal antibodies and mRNA therapies, fostering the dawn of personalized medicine. As we conclude this chapter, we are presented with a dynamic tableau of the pharmaceutical landscape, characterized by unprecedented advancements and promising prospects. This exploration serves as a testament to the pharmaceutical field's unwavering commitment to innovation and its profound impact on healthcare as we navigate the horizon of future trends.

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