Review

Advances and Challenges in IoT-Based Smart Drug Delivery Systems: A Comprehensive Review

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Abstract: In the current era of technology, the internet of things (IoT) plays a vital role in smart drug delivery systems. It is an emerging field that offers promising solutions for improving the efficacy, safety, and patient compliance of drug therapies. IoT-based drug delivery systems leverage advanced devices, sophisticated sensors, and smart tools to monitor and analyse the health matrices of the patient in real-time, allowing for personalised and targeted drug delivery. This technology is implemented through various types of devices, including wearable and implantable devices such as infusion pumps, smart pens, inhalers, and auto-injectors. However, the development and implementation of IoT-based drug delivery systems pose several challenges, such as ensuring data security and privacy, regulatory compliance, compatibility, and reliability. In this paper, the latest research on smart wearable devices and its analysis are addressed. It also focuses on the challenges of ensuring the safe and efficient use of this technology in healthcare applications.

Keywords: healthcare IoT; internet of things; wireless drug delivery; wearable smart drug delivery devices; wireless body area networks (WBANs)

1. Introduction

A drug delivery system refers to the method and route by which a drug is delivered to the site where it will act in the body to show its treatment efficacy. Effective drug delivery requires a multidisciplinary approach and a comprehensive understanding of the drug's properties and the targeted site. However, the lack of targeted delivery limits its efficacy and bioavailability [1]. A collaborative effort between pharmacologists, biologists, chemists, and engineers is required to optimise drug delivery and disease detection [2]. Drug delivery systems comprise various technologies and strategies that are formulated with the objective of conveying therapeutic agents to their targeted site of action within the human body. These systems employ diverse strategies and pathways of administration that are customised to suit the distinctive requirements of the medication and the targeted therapeutic region. Oral delivery, through tablets, capsules, or liquids, is the most common and convenient method. Injectable delivery allows for precise dosage control and rapid absorption when administered subcutaneously, intramuscularly, intravenously, or intra-arterially. Topical delivery involves applying medications to the skin or mucous membranes, while inhalation delivery is through aerosols, gases, or powders for direct respiratory system delivery. Transdermal delivery uses patches or devices for consistent drug release. Implantable delivery involves surgical placement for long-term release. Targeted delivery systems accumulate drugs at specific sites, such as tumours or the brain. Smart drug delivery is an innovative approach that amalgamates advanced devices, state-of-the-art sensors, and sophisticated software into drug delivery systems, aiming to optimise drug

efficacy, safety, and patient compliance [3]. Such systems are designed explicitly to release medication automatically based on a patient's health status, thus mitigating human error and ensuring optimal dosing at the right time [4]. It enables personalised medicine by monitoring the patient's health status, allowing for tailored drug dosage and release. Systems can improve medication compliance and reduce the burden of managing complex regimens, a challenge for many patients [5].

The objective of this review article is to analyse and evaluate the various methodologies and technological advancements in IoT-based drug delivery systems This paper deals in great depth with how IoT can be used to monitor patients' critical illnesses and deliver drugs, including a comparison of modern technology to traditional drug delivery methods. It also outlines the problems with technology, drug delivery, and protocol design using IoT, as well as the solutions to the problems and the direction of future study. A comprehensive literature search was conducted using databases such as PubMed, Scopus, and IEEE Xplore using relevant keywords such as "IoT drug delivery", "wearable devices", "implantable devices", "micro and nano-technologies", and "remote patient care" to identify relevant studies published between 2013 and 2023.

Inclusion and Exclusion Criteria: Inclusion criteria were applied to select studies that focused on IoT technology in drug delivery, encompassing wearable devices, implantable devices, and ingestible and remote IoT-based drug delivery approaches. Studies that were not directly related to IoT-based drug delivery or those that did not provide substantial information on their methodology were excluded.

Data Extraction: Relevant information was extracted from the selected studies, including study design, device description, methodologies employed, key findings, limitations, and implications.

Analysis of data: The extracted data were analysed to identify common methodologies used in the development and implementation of IoT-based drug delivery systems. Key themes, technological innovations, challenges, and gaps in the existing literature were identified.

Comparative Analysis: A comparison and the contrast between the methodologies used in different studies, highlighting the strengths and limitations of each approach, was performed along with identifying the patterns, trends, and emerging techniques in IoT-based drug delivery systems.

The paper is organised as follows: Section 1 describes conventional and smart drug delivery systems. Section 2 highlights IoT, healthcare IoT, and its components. The recent applications of smart drug delivery devices are listed and described in detail in Section 3. The related work and its comparative analysis are described in Section 4. Section 5 deals with security issues faced by WSN in healthcare and their prevention. The regulatory aspect of smart drug delivery devices in healthcare is discussed in Section 6. Section 7 depicts the issues and challenges in IoT networks and their solutions mentioned in Section 8. Section 9 lists the future prospects of smart drug delivery, and Section 10 concludes the paper.

2. Internet of Things and Healthcare IoT

IoT, an acronym for "internet of things", is a network of physical technologies that use in-built sensors, software, and connectivity to exchange data. It allows devices to communicate and perform tasks without human intervention. IoT can revolutionise industries by improving efficiency, automating tasks, and providing novel data analysis. IoT-based drug delivery systems optimise efficiency, accuracy, and safety through smart devices, remote control, and real-time data analysis [6]. Wireless drug delivery, also known as wireless drug administration, refers to a technology-based method for delivering drugs or medications to a patient without the need for physical connections or wires. This can be accomplished through the use of implantable devices, such as pumps or ports, that can receive commands from a remote control or other device to dispense the appropriate amount of medication [7]. Figure 1 shows the process of drug delivery on demand based on IoT. Such devices offer a promising solution to enhance healthcare facilities' operations by ensuring accurate and timely drug administration, continuous monitoring of patients, and improving patient

outcomes [8]. They enable physicians to focus on other critical tasks, provide valuable data for informed decisions, and enhance the quality of healthcare.
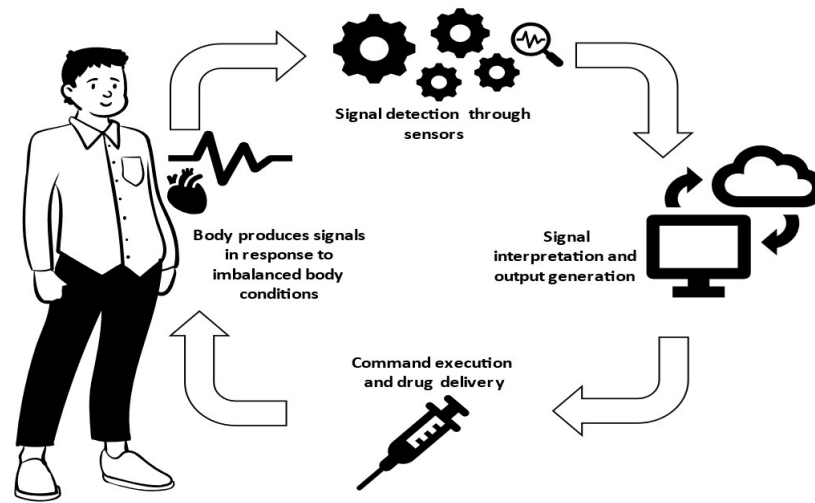

Figure 1. Process of drug delivery on demand based on IoT.

2.1. Healthcare IoT

Healthcare IoT, or the internet of things in healthcare, is the integration of connected technology in the medical industry to collect and exchange data for improved patient care and better decision making. Examples of healthcare IoT devices include wearable fitness trackers, smart pills, and remote supervision devices. The data collected is used by healthcare providers to diagnose the patient's health and plan their care, leading to more personalised, effective, and efficient treatment. Additionally, healthcare IoT can reduce costs and increase efficiency within the healthcare system by reducing the need for in-person appointments. Figure 2 shows different elements in an IoT-based system [9].
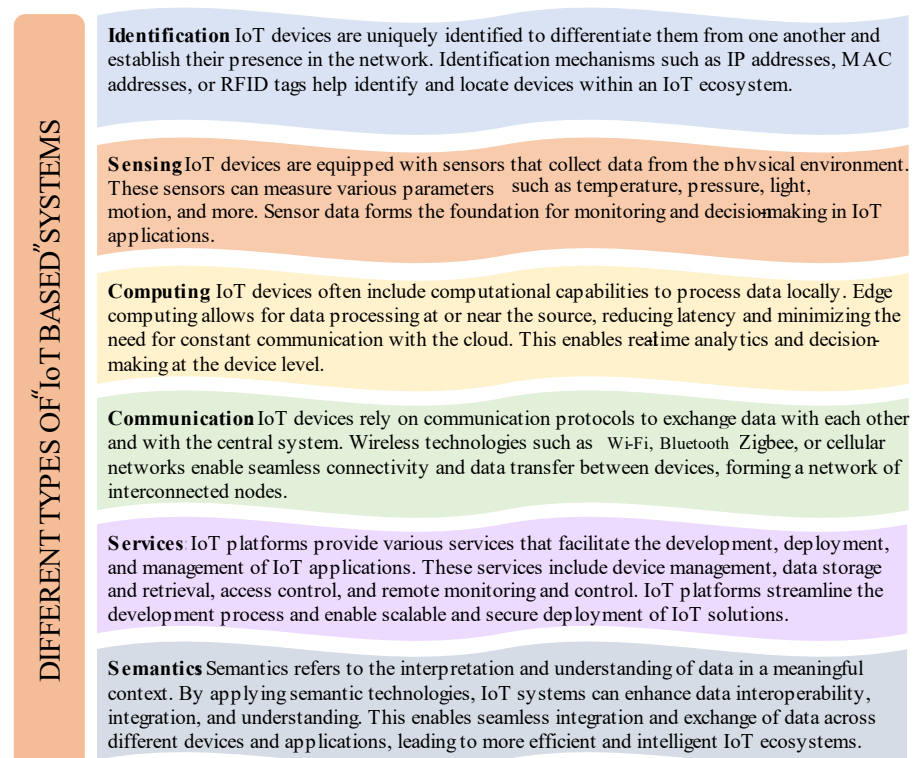

**Figure 2.** Elements of IoT-based system.

Wireless sensor network (WSN): Wireless sensor networks (WSNs) collect data from the environment using small, low-power sensors with wireless communication. They are used in industrial, agricultural, and environmental monitoring systems and measure physical parameters such as temperature, humidity, pressure, motion, and sound. The data are wirelessly transmitted to a central unit for analysis, making it efficient. WSNs serve as sensors, providing data to IoT platforms. Continuous monitoring through WBANs can detect emergencies and diseases early, improving healthcare for people with disabilities and children. Data are wirelessly sent to a monitoring device, which analyses and controls drug delivery, ensuring patients receive the required medication. WBANs benefit drug delivery by improving patient compliance, reducing costs, and increasing healthcare accessibility [10]. Wireless body area networks (WBANs) are a type of wireless sensor network (WSN) system that employs wearable or implanted sensors to collect real-time data on a patient's physiological parameters and clinical metrics [10]. These data are wirelessly transmitted to a central monitoring device that analyses it and remotely controls the drug delivery system, ensuring patients receive the required medication in the right dosage at the right time. WBANs provide numerous benefits in drug delivery, including improved patient compliance, reduced healthcare costs, and increased accessibility to healthcare services [11]. However, their implementation presents challenges such as security, privacy, and interoperability. WBANs can be implemented in wearable or implanted drug delivery systems, with the former delivering medication through a patch or infusion and the latter delivering medication directly to the target area. The communication in a WBAN typically consists of three tiers [12], as given in Figure 3.
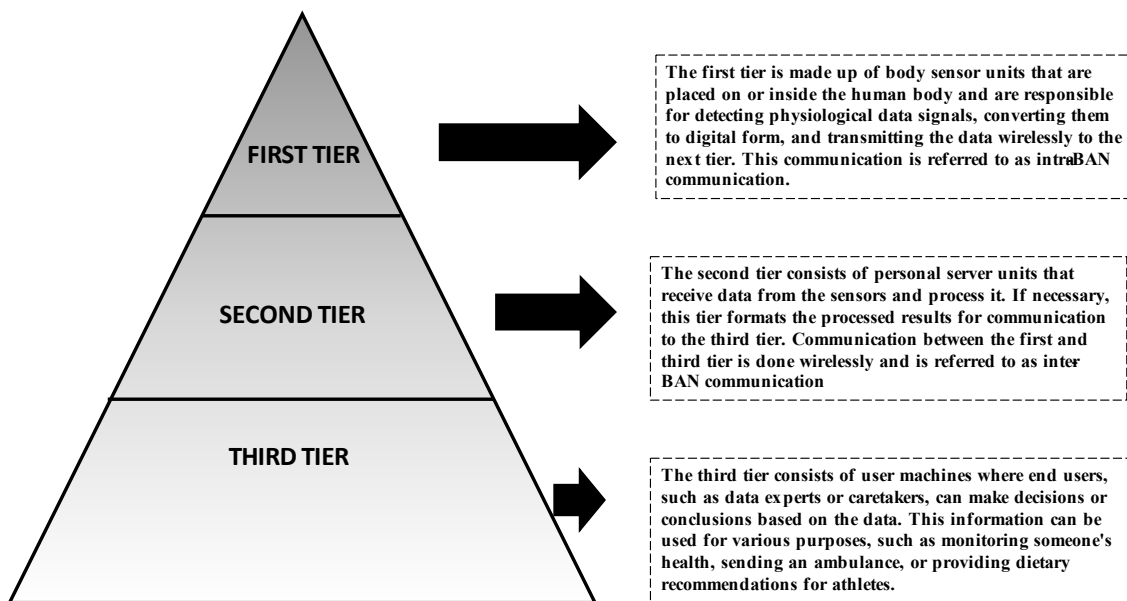
Figure 3. Different tiers of communication in WBAN.

2.2. Body Sensors

Body sensors are the devices that collect the data and transmit them to the network. They can be small and compact and can be placed in various locations to gather data. Figure 4 shows body sensors that are commonly used in health management settings.
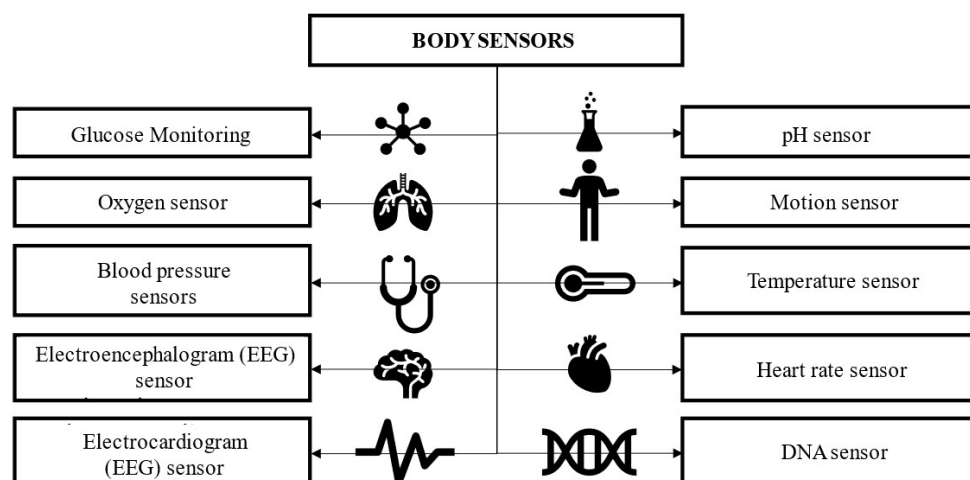
Figure 4. Body sensors commonly used in healthcare applications.

Sensors integrated into drug delivery systems enable real-time monitoring of various physiological parameters, drug levels, or biomarkers. This data can be used to adjust drug dosing or personalise treatment regimens. For instance, glucose sensors can be combined with insulin pumps to create closed-loop systems (also known as artificial pancreas systems), where blood glucose levels are continuously monitored and insulin delivery is automatically adjusted based on the real-time measurements [13].

3. Applications of Smart Drug Delivery Devices

IoT-based drug delivery systems are becoming increasingly popular in the healthcare sector due to their potential to enhance the accuracy, efficiency, and effectiveness of drug delivery. In smart drug delivery systems, various algorithms are involved to analyse data, make intelligent decisions, and optimise treatment. Closed-loop control algorithms are used in systems such as closed-loop insulin delivery for diabetes management, where real-time sensor data are continuously monitored and analysed to determine the appropriate drug dosage or delivery rate. Pharmacokinetic and pharmacodynamic algorithms utilise mathematical models to optimise dosing regimens and predict drug responses based on factors such as drug absorption, distribution, metabolism, and excretion. Machine learning algorithms can analyse large datasets to identify patterns or correlations that inform drug dosing decisions and optimise treatment outcomes. These algorithms enable personalised dosing recommendations, adaptive dosing adjustments, and real-time alerts, enhancing the effectiveness and safety of drug delivery systems [14]. Smart drug delivery systems hold significant potential in improving medication compliance and reducing the burden of complex regimens. IoT-based systems provide unique advantages for smart drug delivery, leveraging their connectivity and seamless data exchange capabilities. With real-time monitoring and data analytics, IoT sensors continuously track drug delivery parameters, patient responses, and environmental factors, enabling prompt intervention and optimised treatment protocols [3]. Remote access and connectivity allow healthcare providers to remotely monitor patient progress, making them particularly valuable for chronic disease management and telemedicine services. Enhanced patient engagement through mobile apps, wearables, and interactive interfaces empowers patients to actively participate in their treatment, leading to improved self-management and treatment outcomes [13]. The scalability and interoperability of IoT infrastructure enable seamless integration with existing healthcare systems, allowing smart drug delivery systems to adapt to evolving needs. Predictive maintenance and data-driven insights optimise system reliability, resource allocation, and workflow efficiency. The classification of IoT-based drug delivery systems is shown in Figure 5.
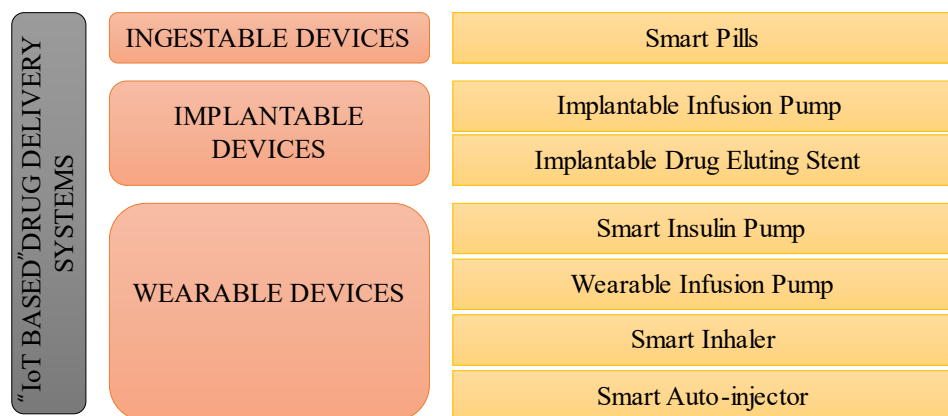
Figure 5. Types of IoT-based drug delivery system.

3.1. Wearable Smart Drug Delivery Devices

IoT-based wearable drug delivery devices are innovative solutions for healthcare, leveraging technology to improve delivery accuracy and efficiency. Worn on the body, like a patch or wristband, health devices track vital indicators and administer medication based on collected data. The devices aid medication adherence for patients with chronic conditions, reducing the risk of adverse events occurring.

3.1.1. Smart Insulin Pens

Smart insulin pens use IoT technology to track and manage insulin delivery for diabetes patients. They transmit dosage and schedule information wirelessly, helping providers monitor treatment. Smart insulin pens provide precise dosing based on blood sugar levels, time, and activity, preventing health complications. Smart insulin pens can help diabetics manage their condition by providing insightful data about their insulin usage [15]. By tracking doses and blood sugar levels, users can detect patterns and receive tailored recommendations for treatment and lifestyle modifications with the associated mobile app. The branded smart insulin pens that are available commercially, and their limitations, are listed in Table 1.

Table 1. List of smart insulin pens available in the market.

Ref.	Brand Name	Name	Key Features	Limitations
[16]	Companion Medical	InPen	Insulin dose calculation with integrative diabetes management app.	Cost (around $699), incompatible with such as U-200 Humalog-, Toujeo-, or Tresiba-type insulin, limited data sharing, and device dependency.
[17]	Novo Nordisk	NovoPen® 6 and NovoPen Echo® Plus	Insulin dose calculation with integrative diabetes management app.	Compatibility: Novo Nordisk's insulin products, including NovoRapid, Levemir, and Tresiba. No dose memory and no automatic dose calculations.
[18]	Lilly	Tempo Pen®	Records the time and dose of each injection and syncs data with the connected diabetes management app.	Limited dose accuracy, limited compatibility (only with insulin produced by Eli Lilly, including Humalog, Humulin, and Basaglar), no data tracking, no dose memory.

Table 1. *Cont.*

Ref.	Brand Name	Name	Key Features	Limitations
[19]	Bigfoot Biomedical	Bigfoot Unity™	A smart insulin pen cap that tracks insulin doses, wirelessly transmits data to a mobile app, and provides personalised insulin dosing recommendations.	No remote monitoring, US-only availability, limited customisation.
[20]	Pendiq	Pendiq 2.0 Insulin Pen	Calculates insulin doses, stores insulin and glucose data, and transmits data wirelessly to a connected mobile device.	Limited European availability, higher cost, compatibility.
[21]	Common Sensing	Gocap Smart Cap	A smart cap that fits on most disposable insulin pens and tracks insulin doses, time stamps injections, and wirelessly syncs data with a mobile app for tracking and analysis.	Compatible with insulin pens manufactured by Sanofi, such as the Lantus Solostar pen and the Apidra SoloStar pen.

3.1.2. Wearable Infusion Pumps

Wearable infusion pumps deliver medications through a catheter under the skin. They are portable, discreet, and programmed to administer precise doses at specific times, providing continuous medication throughout the day. Wearable infusion pumps offer convenient and mobile delivery of medication while minimising infection risk by avoiding disturbance to the infusion site. Wearable infusion pumps offer precise dosing and can adjust medication based on real-time glucose levels for personalised treatment. The wearable infusion pumps for smart drug delivery, and their limitations, are listed in Table 2.

Table 2. List of wearable infusion pumps for smart drug delivery.

Ref.	Brand Name	Name	Key Features	Drug Delivered	Limitations
[22]	Tandem Diabetes Care	t: slim X2 Insulin Pump	Wearable insulin pump with touchscreen interface and Bluetooth connectivity.	Insulin	Device recharging required, infection risk, malfunctions.
[23]	Insulet	Omnipod DASH® Insulin Management System	Wireless pump with handheld controller, customizable insulin delivery, waterproof for 72 h.	Insulin	Training required, frequent pod changes.
[24]	Medtronic	SynchroMed™ II Infusion System	Programmable implanted pump for spinal drug delivery.	Pain and spasticity medications	Implant surgery needed, finite battery, complications.
[25]	Zyno Medical	Z-800F Infusion Pump	Portable wearable pump for medication infusion.	Pain medications, chemotherapy, and other medications	Single medication delivery, incompatible with certain medicines.
[26]	Smith's Medical	CADD®-Solis Ambulatory Infusion Pump	Programmable wearable pump that delivers medication via a small, lightweight pump.	Pain medications, chemotherapy, and other medications	Limited mobility, not suitable for all patients.
[27]	Insulet	Omnipod® Horizon™ Automated Glucose Control System	A tubeless, wearable insulin pump that is currently in development for the delivery of both insulin and glucagon to automatically control glucose concentrations in people diagnosed with type 1 diabetes.	Insulin and glucagon for people with type 1 diabetes	Type 1 diabetes only, patient engagement required, medical conditions exclusion.

3.1.3. Smart Inhalers

Smart inhalers are a type of wearable smart drug delivery device that assists individuals with breathing disorders such as asthma and COPD to better manage their symptoms. These devices can monitor a patient's inhaler usage, provide reminders to take medication, and track medication adherence over time. Some smart inhalers are also able to measure lung function and provide feedback to patients and their healthcare providers. The information gathered by intelligent inhalers can be utilised to enhance treatment strategies, enhance patient results, and decrease healthcare expenditure. The smart inhalation devices for drug delivery, and their limitations, are listed in Table 3.

Table 3. List of smart inhalation devices for drug delivery.

Ref.	Brand Name	Device Name	Key Features	Drug Delivered	Limitations
[28]	Teva Pharmaceuticals	ProAir® Digihaler™	Smart inhaler records usage data, automates dosing.	Albuterol for the treatment of asthma and COPD	Age restriction, limited emergency use, maintenance required.
[29]	ResMed	Propeller Health	Inhaler usage tracker and reminder with app integration and customization.	Various inhaler types for the treatment of asthma and COPD	Limited compatibility, needs patients' engagement, limited clinical evidence.
[30]	Adherium	Smartinhaler™	Smart inhaler sensor with app integration, tracking usage, reminders, and notifications.	Various inhaler types for the treatment of asthma and COPD	Inhaler compatibility, limited feedback, dependence.
[31]	CoheroHealth	HeroTracker® sensors	Wireless sensors track inhaler medication usage automatically and support most inhaler types.	Various inhaler types for the treatment of asthma and COPD	Limited battery life, limited data sharing.

3.1.4. Smart Auto-Injectors

Smart auto-injectors are programmable medical devices that are designed to automatically inject a specific dose of medication. They are also equipped with IoT technology which enables them to connect to other devices or networks and share data in real-time. The IoT-enabled smart auto-injectors are used to administer various types of medication, such as insulin, epinephrine, and other types of drugs. They can be pre-programmed to deliver medication at a specific time or when certain physiological parameters are detected, such as glucose levels in the case of diabetes patients. Table 4 shows some examples of smart auto-injectors for drug delivery.

Table 4. List of smart auto-injectors for drug delivery.

Ref.	Brand Name	Device Name	Key Features	Drug Delivered	Limitations
[32]	Amgen	Neulasta Onpro Kit	Smart auto-injector treats neutropenia during chemotherapy with companion app control.	Pegfilgrastim for the treatment of neutropenia	SubQ only, cost, reliability issues.
[33]	Teva Pharmaceuticals	Ajovy Autoinjector	Smart auto-injector for migraine treatment, controlled by companion app.	Fremanezumab for the treatment of migraines	Potential side effects, proper usage required.
[34]	AbbVie	Humira Citrate-Free Pen	Auto-injector for treating autoimmune conditions, controlled by companion app.	Adalimumab for the treatment of autoimmune conditions	Not compatible with other drug treatment, expensive, side effects experienced.
[35]	Eli Lilly and Company	Trulicity Pen	A smart auto-injector for type 2 diabetes, with medication tracking and reminders.	Dulaglutide for the treatment of type 2 diabetes	Drug-specific use, side effects.

3.2. Implatable Smart Drug Delivery Devices

IoT (internet of things)-based implantable drug delivery devices are a growing trend in the healthcare industry, offering new and innovative solutions for drug delivery. These devices leverage IoT technology to provide real-time monitoring and control of drug delivery, improving the accuracy and efficiency of the delivery process.

3.2.1. Implantable Infusion Pumps

These devices are implantable pumps that can deliver drugs, such as pain medications or chemotherapy, directly to the site of action. The pumps can be controlled wirelessly using a smartphone or other device, allowing healthcare providers to adjust the delivery rate as needed.

Implantable sensor-based infusion pumps are medical devices that are surgically implanted into the body to deliver precise doses of medication, such as insulin for the treatment of diabetes or pain medication for the management of chronic pain. These devices are equipped with sensors that can monitor the patient's physiological parameters and adjust the delivery of medication accordingly. Some examples of implantable sensor-based infusion pumps are given in Table 5.

Table 5. Implantable sensor-based infusion pumps for drug delivery.

Ref.	Brand Name	Device Name	Key Features	Drug Delivered	Limitations
[36]	Abbott	Infinity™ Deep Brain Stimulation (DBS)	Implantable infusion pump for deep brain stimulation therapy in Parkinson's.	Various medications, such as levodopa for the treatment of Parkinson's disease	Invasive procedure, possible neurological side effects, frequent follow-up.
[37]	B. Braun Medical	Infusomat Space	Implanted pump delivers medication to specific body areas for various conditions.	Various medications, such as opioids for pain management	Compatibility limitations, requires specialised training, susceptible to error.

3.2.2. Implantable Drug-Eluting Stents

These are stents that are implanted in blood vessels to deliver drugs, such as anti-inflammatory or anti-proliferative agents, directly to the site of action. The stents can be controlled wirelessly using a smartphone or other device, allowing healthcare providers to adjust the delivery rate as needed. A list of some examples of implantable drug-eluting stents is given in Table 6.

Table 6. List of implantable drug-eluting stent.

Ref.	Brand Name	Device Name	Key Features	Drug Delivered	Limitations
[38]	Abbott	Xience Sierra™	Implantable stent with drug coating and remote monitoring for artery treatment.	Everolimus, an immunosuppressant medication, for the prevention of restenosis after coronary artery angioplasty	Complications and potential re-treatment needed.
[39]	Medtronic	Resolute Onyx™	Implantable stent with polymer coating and remote monitoring to prevent re-narrowing.	Zotarolimus, an immunosuppressant medication, for the prevention of restenosis after coronary artery angioplasty	Expertise required, risk of complications with some medications.
[40]	Boston Scientific	Promus PREMIER™	Remote monitoring, drug-eluting, artery stent for preventing re-narrowing with app.	Everolimus, an immunosuppressant medication, for the prevention of restenosis after coronary artery angioplasty	Late complications, limited options.

3.3. Ingestible Smart Drug Delivery Devices

IoT-based ingestible smart drug delivery devices are another growing trend in the healthcare industry. These devices leverage IoT technology to provide real-time monitoring and control of drug delivery, improving the accuracy and efficiency of the delivery process. Some examples of IoT-based ingestible smart drug delivery devices are given in Table 7.

Table 7. Smart pills for drug delivery and vitals monitoring.

Ref.	Brand Name	Device Name	Key Features	Drug Delivered	Limitations
[41]	Proteus Digital Health	Abilify MyCite®	Ingestible pill with sensor and wearable patch for medication adherence monitoring and health data tracking.	Aripiprazole, an antipsychotic medication	Limited availability, privacy, cost.
[42]	etectRx	ID-Cap™ System	Smart pill with sensor sends data to wearable and smartphone, tracking medication adherence, heart rate, and temperature.	Various medications, including antibiotics, painkillers, and anticoagulants	Limited battery life, the transmission distance between the reader and the sensor is limited, patient non-compliance.

4. Research Survey for Exploring the Role of IoT in Revolutionising Healthcare

IoT technology improves drug delivery by allowing real-time monitoring, personalised dosing, and remote patient care. Studies have explored IoT drug delivery for chronic disease, cancer, and pain management, with the literature examining technical, clinical, and regulatory challenges.

In research conducted in 2020 [43], a laboratory syringe pump was developed as an open-source solution using Arduino UNO and an LCD keypad shield for easy device interaction and setting changes without a computer connection. The device infused fluids and refilled syringes. Analysing a 10 mL syringe showed a systematic error of 0.1% and a random error of 3 L for dispensed volumes of 1–5 mL. In another study [44], a new wearable and disposable glucose monitoring device that used sweat for non-invasive measurement, which included pH, temperature, and humidity measurements for real-time glucose level correction, contained temperature-responsive nanoparticles in hyaluronic acid hydrogel microneedles. This innovation offered non-invasive diabetes mellitus treatment by monitoring glucose through sweat analysis.

Bi-hormonal systems aim to prevent low blood sugar events and maintain glucose within the targeted range by delivering both glucagon or amylin and insulin; these were tested in [45]. To enhance islet transplantation, encapsulation strategies were used that promote angiogenesis, oxygen delivery, and immune protection, which eliminate immuno-suppression and enhance long-term survival and function. A new implant delivers drugs precisely using micro- and nano-technologies; a CMOS SoC device combines wireless control, actuation, and drug delivery [46]. This device can be implanted via minimally invasive surgery to treat cancer and heart attacks. Another new drug delivery approach, using a wireless micropump with acoustofluidic technology [47], which was compact, wirelessly controlled, and integrated with technology, miniaturised sensors, and electronics that could create on-demand drug delivery systems. New soft and thin neural probes (MICROFLU-IDIC) that injected drugs precisely into deep brain tissue wirelessly and with high control over time and location were shown in research carried out in 2015 [48]. Using 3D printing, an electrochemical pump with an expandable Parylene C micro-bellows membrane and precise microneedles (100 m diameter, 300 m long) for drug delivery was constructed by Moussi K. in 2019 [49]; it could deliver the drug in 10 s using wireless power up to a 10 mm distance. In a recent study [50], miniaturised heaters with resonant frequencies of 30–100 MHz were equipped with hydrogel, and the temperature was elevated by up to

20 °C, shrinking the hydrogel by 40%. This showed a frequency-controlled release with an active range of 2 MHz. A 2013 [51] drug delivery system injected antiepileptic drugs at the onset of an electrographic seizure to enhance seizure control. The system included a seizure detector, preamplifier, wireless control module, and micropump unit, with emphasis on the micropump prototype. The results indicated that the micropump was precise, low-power, and suitable for implantable use in responsive drug delivery. Researchers also developed a drug delivery system within the IoT that offers real-time medication administration for seizure control [52]. The system used a valveless micropump, powered by electromagnetics and made of flexible polydimethylsiloxane, for precise drug delivery. The authors in [53] introduced an innovative cancer therapy using an IoT-based micropumping device for wireless reconfiguration. This implantable device stored anticancer drugs in refillable reservoirs and allowed remote control and adjustment of drug administration. In vitro tests showed that the system delivered anticancer drugs accurately, inhibiting breast cancer cells by over 71%.

An IoT-based anaesthesia drug control system for monitoring and controlling anaesthesia drugs for patients was designed in [54]. The system detects pulse rate and temperature to adjust anaesthesia. It uses NodeMCU for control. Ubidots cloud allowed medical professionals to monitor patient data via IoT. It showed an efficient solution for anaesthesia control. IV drug administration is effective, but manual setup lacks accuracy and monitoring. Radioactive scan chamber safety concerns led to a clinical survey in 2021 [55] to find an improved device for intravenous drips. This study proposes an IoT-based device to address air embolism and blood backflow and improve drug administration for neonates and paediatrics. The device solves manual IV drip control and offers real-time monitoring.

Wireless controllers are now essential in healthcare, with researchers exploring advanced medical devices for efficient medication delivery. In research work [56], a smartphone-controlled iontophoretic drug delivery device with a hardware module and mobile app for drug delivery control was developed. It features a safety mechanism to detect loose leads and stop drug delivery. The device's performance was tested in an in vitro drug release investigation, yielding promising results for emulsion gel-based drug delivery. India's healthcare sector is important to its economy, but high costs are a concern. AIDD proposes using IoT and ML for an improved insulin delivery system for comatose patients [57]. Multiple ML models were used to predict insulin doses for diabetic patients remotely, eliminating the need for physical assistance. A remote system with interconnected devices that delivers drugs and prognosis was designed in [58]. This system enabled monitoring of patients' vital signs, collecting sensor data, and regulating drug release via an implantable pump. Rigorous testing confirmed the system's effectiveness in remote medical care. In recent times, due to COVID-19, COPD patients in hospitals struggled to receive proper drug injections and monitoring. A system was created with medical devices and IoT technology to provide the necessary oxygen and vital signs monitoring [59]. The system had two sections: one monitored the drip rate and fluid volume using an IR sensor and photodiode, and the other controlled the nebulization speed and duration with an Arduino Nano and MOSFET. This system improved COPD patients' quality of life through better medical care. The authors in [60] proposed an IoT and AI system with fuzzy learning to regulate anaesthesia during surgery. Adaptable and robust to surgical disturbances, a system using sliding mode control, type II fuzzy systems, and artificial neurons was used to regulate anaesthesia drug infusion and adjust the bispectral index. It also allowed for remote drug infusion adjustments. The automated temperature controller (AMTC) was developed in 2021 [61] for synthesising NiO and CuO nanoparticles. The device created dexamethasone-loaded nanomicelles for testing transcorneal penetration. It had the potential for other controlled thermal reactions, providing a compact solution.

In 2015 [62], an implanted micropump device using electrolysis, EI sensors, and wireless technology for drug delivery was formulated. This system was tested successfully for controlled infusion rate, sensed dosage in simulated brain tissue, and estimated coil

separation and off-centre. RFID tags with helical antennas and drug compartments for tracking drug dosage in real-time were created, with two prototypes being tested to monitor drug dosage changes in vitro [63]. The results showed a sensitivity of 1.27 L/MHz for transdermal delivery and 2.76 L/MHz for implanted delivery. Another new approach for anticancer drug delivery to brain tumours with a biodegradable patch and wireless system is described in [64]. Promising results were found in mouse and large animal models, with tumour volume suppression and improved survival rates, indicating the potential for treating brain tumours in humans. The best way to treat medical conditions is with localised and controlled drug release using a wireless implant that is biodegradable and does not require surgical extraction; one such implant was studied in 2015 [65]. The system's efficacy and biocompatibility were proven through in vitro and in vivo studies. Wearable technology measures vital signs, leading to disease control. Closed-loop systems use wearables to deliver drugs for complete control. This text focuses on closed-loop systems and transdermal delivery technologies enabled by digital wearables [66]. A miniaturised dental patch system was developed [67] to monitor the microenvironment and control fluoride treatment for early prevention and management of tooth decay caused by oral biomes. The system utilises near-field communication for wireless data transmission with smart devices attached to the teeth.

In a study performed in 2021 [68], researchers created a wireless, self-powered, and smart wound dressing for infection treatment and supervision. Its flexible electronics detect infestations, deliver medication, and allow for independent monitoring and treatment. This experiment shows potential for closed-loop biomedical systems. An implantable drug delivery device (SID) for neurological emergencies that integrates wirelessly with wearables monitoring EEG signals was designed [69], which, when tested in animals, showed that using the SID reduced brain damage and improved survival rates. In [70], wearable devices delivered drugs via the skin with electrical control. The drug is administered through a paper electrode with polypyrrole and sodium salicylate. Using different potentials, this device controlled drug release dose and rate, making it ideal for closed-loop delivery and the detection of various illnesses. In another study [71], an electro-drug system for the GI tract with a capsule containing drugs, sensors, wireless capabilities, and motors was developed. Twenty healthy volunteers underwent two observational studies to evaluate the safety and functionality of the ingested capsule. In another study, 99 mTc was expelled remotely from the capsule and tracked by scintigraphy. The results showed that the capsule was safe and well tolerated, with successful transmission of temperature and pH data in 96.5% of cases. The 99 mTc was successfully removed remotely in 9 of 10 subjects, and its location correlated with scintigraphy based on pH. The wireless system [72] remotely powered the implanted device, controlling the dose rate with voltage and resistance adjustments. Proof-of-concept for the system's feasibility and controllability was demonstrated with liquid and solid drugs. The results showed consistent flow rates and steady dose release, even with a solid drug substitute. A new approach [73] integrated sensors with drug delivery devices using carbon ink embedded in PDMS membranes for accurate volume monitoring. The device delivers 7 L of drug solution with a 6.5% accuracy.

Contemporary research has advanced multiple potential methodologies for drug delivery that encompass diverse approaches, such as wearable and disposable glucose monitoring devices, bi-hormonal systems, encapsulation strategies, implantable devices exploiting micro- and nano-technologies, pliable and slender neural probes, 3D printing, frequency-controlled release, valveless micropumps, and iontophoretic drug delivery devices, which could potentially be employed for anaesthesia regulation, intravenous drips, insulin delivery, remote medical care, chronic obstructive pulmonary disease patient monitoring, etc. The utilisation of wireless controllers, cloud computing, and machine learning algorithms has facilitated the expansion of remote patient monitoring and drug administration. Existing studies and their limitations are listed in Table 8.

Table 8. Comparative studies of IoT-based drug delivery systems.

Ref.	Year	Technology	Communication Protocols	Limitations
[23]	2023	Implantable micropump	UART (universal asynchronous receiver/transmitter)	More testing needed for antiepileptic injection.
[24]	2019	Micropumping system	Not specified	EEG seizure detection limitations, lacks clinical trials.
[25]	2021	Reconfigurable micropump	HTTP (hypertext transfer protocol)	System requires further in vivo testing.
[28]	2021	Servomotor driven by NodeMCU-based control system.	ZigBee	70 m outdoor, 30 m indoor range.
[32]	2020	Closed-loop remote medical system (wireless implantable pump)	MQTT (message queuing telemetry transport)	Low-frequency signal limits information transmission, limited power signal distance.
[34]	2015	Micropump with integrated dosing sensors	Bluetooth	Micropump may not support certain drugs, small reservoir.
[35]	2014	Miniaturized helix antennas	RFID (radio frequency identification)	Power-hungry components may limit range.
[39]	2020	Intraoral theranostic wearable system	Near-field communication (NFC)	Smartphones may lack NFC capability, unreliable energy transfer.
[42]	2020	A near-field communication smartphone, a wireless battery-free wearable device, and pliable circuit board	NFC (near-field communication module)	PPy electrode limits drug delivery, limited range.
[44]	2017	Implantable electrolytic actuator pump	R-WPT	Limited flow rate control.

5. Security Issues in Wireless Sensor Networks Used in Healthcare

Security is a critical aspect of WSNs, as they can be vulnerable to hacking or unauthorised access. Effective security measures such as encryption and authentication are, therefore, essential to ensuring the accuracy of the data collected by the sensors. Figure 6 gives different security issues with WSNs used in healthcare [74–79].
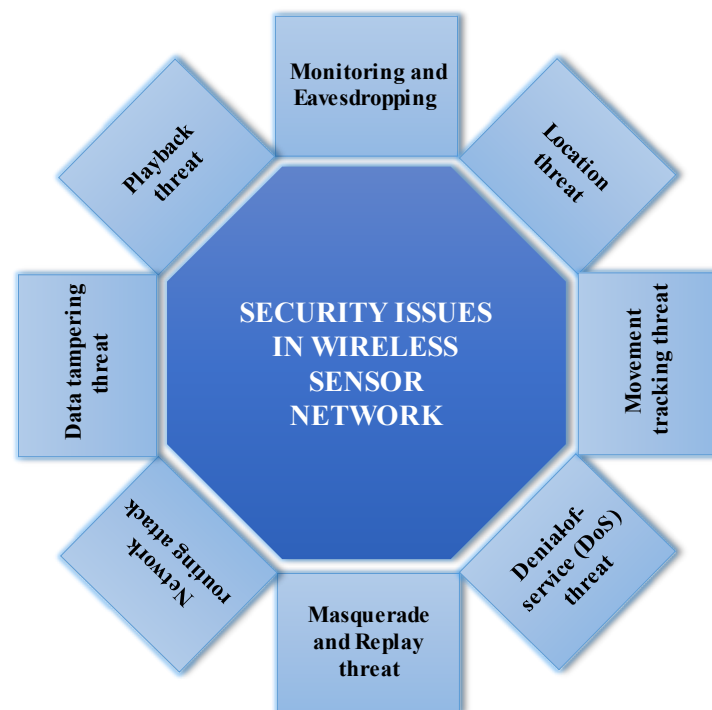
Figure 6. Security issues in a wireless sensor network.

Wireless medical sensor networks (WMSNs) face various security risks that can compromise patient confidentiality and the integrity of data transmission. Unauthorised surveillance and interception of patient data, along with the manipulation or tampering of transmitted data, pose significant threats [74]. Routing attacks targeting wireless sensor networks can disrupt communication and lead to the loss of sensitive information. Masquerade and replay threats involve unauthorised entities impersonating authentic nodes or replaying intercepted data, compromising data credibility. Location and movement tracking threats can reveal the location of sensor nodes and patients, jeopardising privacy and safety. Denial-of-service (DoS) attacks can disrupt network operations, causing delays in critical data transmission. Implementing secure communication protocols, encryption, authentication, and network monitoring systems is essential to mitigate these threats and ensure the security and privacy of wireless healthcare systems [75–79].

Preventing security issues in wireless sensor networks (WSNs) used in healthcare is crucial to protecting patient privacy, preventing medical errors, and maintaining trust. Measures to prevent these issues include data validation to ensure authenticity and integrity, data privacy to protect against unauthorised access and disclosure, and data reliability to prevent alteration during transmission. Key exchange protocols ensure secure communication, while role-based access control mechanisms restrict data access to authorised personnel. Accurate location estimation, user verification, and informed consent protocols further enhance security. Additionally, ensuring data timeliness, managing processing overhead, and implementing post-compromise security measures are essential. By implementing these preventive measures, healthcare organisations can safeguard patient data, maintain data availability, and protect against reputational damage and adverse health outcomes [80].

6. Regulatory Frameworks

Regulatory frameworks and guidelines for ensuring data security in IoT-based drug delivery systems vary across different countries and regions. Some notable examples include the general data protection regulation (GDPR) in the European Union, which sets guidelines for data collection and processing, and the United States Food and Drug Administration (FDA) guidelines, which address cybersecurity considerations for medical devices [81]. The National Institute of Standards and Technology (NIST) provides cybersecurity guidelines applicable to IoT devices, while the International Medical Device Regulators Forum (IMDRF) offers guidance on cybersecurity for medical devices. The European Medical Device Regulation (MDR) and Underwriters Laboratories (UL) also provide requirements and standards for ensuring the security of IoT-based systems. The threats faced by IoT drug delivery systems include data breaches, unauthorised access, and the potential compromise of patient information. To overcome these threats, manufacturers and stakeholders must implement robust security controls, encryption mechanisms, access controls, and regular software updates to mitigate vulnerabilities and protect the confidentiality, integrity, and availability of data. Ongoing monitoring, compliance with regulatory frameworks, and staying informed about emerging threats and best practices are crucial for maintaining data security in IoT-based drug delivery systems.

7. Issues and Challenges

Implementing the IoT in drug delivery systems is a complex and challenging task that requires addressing several issues. Addressing these challenges is crucial for the successful deployment of IoT-based drug delivery systems, which can revolutionise the healthcare industry by providing more precise and effective treatments to patients. IoT-based drug delivery systems have the potential to significantly improve patient care and treatment outcomes by providing personalised and timely medication delivery. However, integrating these devices with the existing healthcare infrastructure can be challenging, as there are often several different systems and technologies in place. This can lead to interoperability

issues, which can be seen by the lack of standardization and compatibility among devices. Some issues faced by IoT-based drug delivery systems are:

- Data security: robust security measures must be in place to prevent unauthorised access and data breaches.
- Regulatory standards: stringent regulatory standards must be met to ensure patient safety and efficacy.
- Ethical and social implications: ethical and social implications must be addressed through discourse to align with societal values and goals.
- Device reliability and accuracy: IoT devices must be reliable and accurate to ensure patient safety and treatment efficacy.
- Standardisation and compatibility: standardisation and compatibility are crucial for seamless communication and collaboration among devices, sensors, and platforms.
- Limited connectivity: limited connectivity can result in devastating patient consequences, and low latency must be taken into consideration in healthcare.
- High costs of adoption: the high costs of development, manufacturing, and adoption present a significant financial challenge for companies looking to enter this market.
- Inadequately trained IT departments: IT departments may struggle with managing safety, security, and maintenance when dealing with a large influx of IoT devices during implementation.

8. Solution of Challenges

IoT-based drug delivery presents a number of challenges that must be overcome in order to fully realise its potential. One of the most critical challenges is ensuring the security and privacy of patient data. This requires the development of robust security measures, including encryption, authentication, and access control, to safeguard patient information from unauthorised access or data breaches. Interoperability and standardisation of IoT devices and platforms are also necessary to improve compatibility and facilitate seamless communication between devices, ultimately reducing costs and improving performance.

Another challenge is compliance with regulatory frameworks to ensure patient safety and build trust in the technology. This includes adhering to various regulations and standards such as HIPAA, GDPR, and ISO 13485, which provide guidelines for data privacy, security, and quality management. Additionally, the accuracy and reliability of IoT devices must be ensured through testing and validation processes to ensure the technology can be relied upon to deliver effective and safe healthcare.

To manage the deployment and maintenance of IoT devices, healthcare organisations must invest in adequate staffing and training. This can help to ensure that the devices are managed properly and patient data remains secure and confidential. Ethical and social considerations should also be addressed to ensure that IoT-based drug delivery systems align with the values and needs of patients, healthcare providers, and other stakeholders.

While the benefits of IoT-based drug delivery are clear, the cost of developing and implementing such systems can be a significant barrier for many healthcare organisations. To manage costs, it is crucial to adopt better approaches to cost modelling, outlining the expenses associated with hardware and software architectures, and ensuring proper cost estimation.

Connectivity and reliability are also crucial for IoT-based drug delivery systems. Designers must prioritise connectivity and testing during the early stages of development to ensure that the devices can function continuously without any failures. The use of fog computing can also help to reduce data processing delays that can occur due to the long distance between IoT sensors and data processing devices. By providing faster data processing and reducing reliance on cumbersome cloud storage, fog computing can improve the quality of service and make the IoT more useful for healthcare by allowing doctors to make better-informed decisions.

9. Future Prospects

The future prospects of IoT-based drug delivery systems are vast and promising. These systems can revolutionise the healthcare industry by improving patient outcomes and transforming healthcare delivery. With advancements in technology and the increasing demand for personalised medicine, IoT-based drug delivery can offer a tailored approach to treatment, resulting in enhanced patient care. The integration of IoT devices with drug delivery systems can provide real-time monitoring of patient health, enabling healthcare professionals to adjust treatments accordingly, leading to improved patient outcomes. Moreover, IoT-based drug delivery can also increase the efficiency and accuracy of drug administration, resulting in reduced medication errors and improved patient compliance.

These systems can also facilitate remote monitoring of patients, enabling healthcare providers to track and monitor patients' health status from afar, making healthcare delivery more accessible and efficient. The proliferation of IoT devices and the growing demand for connected healthcare have opened up new opportunities for the development of innovative IoT-based drug delivery systems. These systems can leverage the power of machine learning and predictive analytics to offer real-time insights into patient health and optimise drug delivery, resulting in better patient outcomes. In addition, the deployment of IoT-based drug delivery systems can generate vast amounts of data, which can be leveraged to improve clinical research and drug development. These systems can facilitate the collection of patient data in real-time, allowing for the analysis of large datasets and the identification of trends and patterns that could inform drug development and research. Overall, the future prospects of IoT-based drug delivery systems are vast, and the integration of these systems with other emerging technologies, such as artificial intelligence and blockchain, can offer even more exciting opportunities for the healthcare industry. As technology continues to evolve and become more accessible, we can expect to see IoT-based drug delivery systems becoming more prevalent and transforming the way we deliver healthcare.

10. Conclusions

The current and future prospects of IoT-based drug delivery systems are promising. The integration of IoT networks with drug delivery systems has transformed drug delivery and monitoring, enabling healthcare providers to deliver medication more accurately, efficiently, and safely. IoT-based drug delivery systems have the potential to revolutionise patient care by improving medication adherence, personalised dosing, and remote monitoring. Wearable devices and smart pills can provide real-time data on patients' vital signs and drug uptake, enabling healthcare providers to adjust dosages and treatment plans accordingly. Implantable devices can provide continuous monitoring and drug delivery, allowing patients to manage their conditions better. However, security issues such as hacking, malware, and data breaches pose a significant challenge in implementing IoT-based drug delivery systems. It is crucial to establish robust security protocols to safeguard patient privacy and data. The future of IoT-based drug delivery systems looks promising, with ongoing research and development focused on developing more advanced devices and improving security protocols. Advanced implantable sensors and artificial intelligence integration are some of the areas of ongoing research. In conclusion, IoT-based drug delivery systems hold significant potential for improving patient outcomes, enhancing medication adherence, and reducing healthcare costs. With continued investment and innovation, these systems will undoubtedly transform the healthcare industry in the coming years.

References

1. Bachmann, K. Drug metabolism. In *Pharmacology*; Hacker, M., Messer, W., Bachmann, K., Eds.; Academic Press: Cambridge, MA, USA, 2009; pp. 131–173.

2. Cupić, M.; Lazarević, I.; Knezević, A.; Stanojević, M. Conventional and molecular methods in diagnosis and monitoring of viral infection. *Srp. Arh. Celok. Lek.* **2007**, *135*, 589–593.

3. Liu, D.; Yang, F.; Xiong, F.; Gu, N. The Smart Drug Delivery System and Its Clinical Potential. *Theranostics* **2016**, *6*, 1306–1323. [CrossRef]

4. Domingo-Lopez, D.A.; Lattanzi, G.; Schreiber, L.H.J.; Wallace, E.J.; Wylie, R.; O'Sullivan, J.; Dolan, E.B.; Duffy, G.P. Medical devices, smart drug delivery, wearables and technology for the treatment of Diabetes Mellitus. *Adv. Drug Deliv. Rev.* **2022**, *185*, 114280. [CrossRef]

5. Mun, L.B.; Jinsong, O. Intelligent healthcare service by using collaborations between iot personal health devices. *Int. J. Bio-Sci. Bio-Technol.* **2014**, *6*, 155–164.

6. Hao, Y.; Khan, A.N.; Ermakov, A.; Sukhorukov, G. Wireless Drug Delivery Devices. In *Antenna and Sensor Technologies in Modern Medical Applications*; IEEE: Piscataway, NJ, USA, 2021; pp. 319–344.

7. Shafiq, M.; Gu, Z.; Cheikhrouhou, O.; Alhakami, W.; Hamam, H. The Rise of "Internet of Things": Review and Open Research Issues Related to Detection and Prevention of IoT-Based Security Attacks. *Wirel. Commun. Mob. Comput.* **2022**, *2022*, 8669348. [CrossRef]

8. Zamanifar, A. Remote patient monitoring: Health status detection and prediction in IoT-based health care. In *IoT in Healthcare and Ambient Assisted Living*; Springer: Berlin/Heidelberg, Germany, 2021; pp. 89–102.

9. Yousefnezhad, N.; Malhi, A.; Främling, K. Automated IoT Device Identification Based on Full Packet Information Using Real-Time Network Traffic. *Sensors* **2021**, *21*, 2660. [CrossRef]

10. Taslim Arefin, M.D.; Mohammad, H.; Haque Fazlul, A.K.M. Wireless Body Area Network: An Overview and Various Applications. *J. Comput. Commun.* **2017**, *5*, 53–64. [CrossRef]

11. Rathee, D.; Rangi, S.; Chakarvarti, S.K.; Singh, V.R. Recent trends in Wireless Body Area Network (WBAN) research and cognition based adaptive WBAN architecture for healthcare. *Health Technol.* **2014**, *4*, 239–244. [CrossRef]

12. Morales-Sandoval, M.; De-La-Parra-Aguirre, R.; Galeana-Zapien, H.; Galaviz-Mosqueda, A. *A Three-Tier Approach for Lightweight Data Security of Body Area Networks in E-Health Applications*; IEEE Access: Cambridge, MA, USA, 2021; Volume 9, pp. 146350–146365. [CrossRef]

13. Saunders, A.; Messer, L.H.; Forlenza, G.P. MiniMed 670G hybrid closed loop artificial pancreas system for the treatment of type 1 diabetes mellitus: Overview of its safety and efficacy. *Expert Rev. Med. Devices* **2019**, *16*, 845–853. [CrossRef]

14. Hassanzadeh, P.; Atyabi, F.; Dinarvand, R. The significance of artificial intelligence in drug delivery system design. *Adv. Drug Deliv. Rev.* **2019**, *151*, 169–190. [CrossRef]

15. Heinemann, L.; Schnell, O.; Gehr, B.; Schloot, N.C.; Görgens, S.W.; Görgen, C. Digital Diabetes Management: A Literature Review of Smart Insulin Pens. *J. Diabetes Sci. Technol.* **2022**, *16*, 587–595. [CrossRef]

16. Medtronic Diabetes. InPen Smart Insulin Pen System. 2023. Available online: https://www.medtronicdiabetes.com/products/inpen-smart-insulin-pen-system (accessed on 19 February 2023).

17. Novo Nordisk A/S. Smart Pens. 2023. Available online: https://www.novonordisk.com/our-products/smart-pens.html (accessed on 19 February 2023).

18. Eli Lilly and Company. Lilly to Begin Rollout of Tempus' Personalized Diabetes Management Platform in the U.S. 21 June 2021. Available online: https://investor.lilly.com/news-releases/news-release-details/lilly-begin-rollout-tempor-personalized-diabetes-management (accessed on 19 February 2023).

19. Bigfoot Biomedical. Bigfoot Unity. 2023. Available online: https://www.bigfootbiomedical.com/bigfoot-unity (accessed on 19 February 2023).

20. Pendiq. Pendiq 2.0 Insulin Pen. 2023. Available online: https://pendiq.com/en/insulin-pen/ (accessed on 19 February 2023).

21. Sangave, N.A.; Aungst, T.D.; Patel, D.K. Smart Connected Insulin Pens, Caps, and Attachments: A Review of the Future of Diabetes Technology. *Diabetes Spectr.* **2019**, *32*, 378–384. [CrossRef]

22. Tandem Diabetes Care. t:slim X2 Insulin Pump. 2023. Available online: https://www.tandemdiabetes.com/products/t-slim-x2-insulin-pump (accessed on 19 February 2023).
23. Insulet Corporation. Omnipod Reviews. 2023. Available online: https://www.omnipod.com/is-omnipod-right-for-me/omnipod-reviews (accessed on 19 February 2023).
24. Medtronic. SynchroMed™ II Programmable Pump. 2023. Available online: https://www.medtronic.com/us-en/healthcare-professionals/products/neurological/drug-infusion-systems/synchromed-ii.html (accessed on 19 February 2023).
25. Zyno Medical. Products—Large Volume Infusion Pump Systems Overview. Available online: https://zynomed.com/Products%20-%20Large%20Volume%20Infusion%20Pump%20Systems%20Overview.html (accessed on 19 February 2023).
26. Smith's Medical. CADD®-Solis Ambulatory Infusion Pump. 2023. Available online: https://www.smiths-medical.com/products/infusion/ambulatory-infusion/ambulatory-infusion-pumps/caddsolis-ambulatory-infusion-pump (accessed on 19 February 2023).
27. Cobry, E.C.; Berget, C.; Messer, L.H.; Forlenza, G.P. Review of the Omnipod® 5 Automated Glucose Control System Powered by Horizon™ for the treatment of Type 1 diabetes. *Ther. Deliv.* **2020**, *11*, 507–519. [CrossRef]
28. Teva Pharmaceutical Industries Ltd. Teva Announces Availability of ProAir® Digihaler® (Albuterol Sulfate) 117 mcg Inhalation Powder for Patients with Asthma and COPD in the United States. 9 August 2021. Available online: https://www.tevapharm.com/news-and-media/latest-news/teva-announces-availability-of-proair-digihaler-albuterol-sulfate-117-mcg-inhalation-powder-for-patie/ (accessed on 19 February 2023).
29. Propeller Health. ResMed to Acquire Propeller Health, Leader in COPD and Asthma Connected Health Solutions, for $225 Million. 3 December 2018. Available online: https://propellerhealth.com/press/press-releases/resmed-acquire-propeller-health-leader-copd-asthma-connected-health-solutions-225-million/ (accessed on 19 February 2023).
30. Adherium. Adherium Smartinhaler Technology in New Multinational Study. 6 September 2016. Available online: https://www.adherium.com/news/adherium-smartinhaler-technology-in-new-multinational-study/ (accessed on 19 February 2023).
31. Cohero Health. Products. Available online: https://coherohealth.com/products/ (accessed on 19 February 2023).
32. Amgen. Neulasta® (Pegfilgrastim). 2022. Available online: https://www.neulasta.com/ (accessed on 19 February 2023).
33. Teva Pharmaceutical Industries Ltd. Teva Announces, U.S. Launch of Autoinjector for AJOVY® (Fremanezumab-vfrm) Injection. 4 June 2020. Available online: https://www.tevapharm.com/news-and-media/latest-news/teva-announces-u-s-launch-of-autoinjector-for-ajovy-fremanezumab-vfrm-injection/ (accessed on 19 February 2023).
34. AbbVie Inc. HUMIRA® (Adalimumab): Now Available without Citrate. Available online: https://www.humira.com/citrate-free (accessed on 19 February 2023).
35. Eli Lilly and Company. Trulicity® (Dulaglutide) Injection, for Subcutaneous Use. 2022. Available online: https://www.trulicity.com/ (accessed on 19 February 2023).
36. Abbott. Parkinson's Disease & Deep Brain Stimulation (DBS) Therapy. Available online: https://www.abbott.com/life-changing-tech/parkinsons-deep-brain-stimulation-dbs-infinity.html (accessed on 19 February 2023).
37. Braun, B.; Melsungen, A.G. Infusomat® Space. Available online: https://www.bbraun.com/en/products/b/infusomat-space.html (accessed on 19 February 2023).
38. Abbott. XIENCE Sierra™ Everolimus Eluting Coronary Stent System. Available online: https://www.cardiovascular.abbott/us/en/hcp/products/percutaneous-coronary-intervention/xience-family/xience-sierra.html (accessed on 19 February 2023).
39. Medtronic Resolute Onyx™ DES. Available online: https://www.medtronic.com/me-en/healthcare-professionals/products/cardiovascular/stents/resolute-onyx-des.html (accessed on 19 February 2023).
40. Boston Scientific. Promus Premier™ Everolimus-Eluting Platinum Chromium Coronary Stent System. IC-262209-AF SEP2015. 2015. Available online: https://www.bostonscientific.com/en-US/products/stents{-}{-}coronary/promus-premier-stent-system.html (accessed on 19 February 2023).
41. Otsuka Pharmaceutical Co., Ltd. Digital Medicine System: ABILIFY MYCITE® (Aripiprazole Tablets with Sensor). 13 November 2017. Available online: https://www.otsuka-us.com/discover/articles-1075 (accessed on 19 February 2023).
42. Flores, G.P.; Peace, B.; Carnes, T.C.; Baumgartner, S.L.; Buffkin, D.E.; Euliano, N.R.; Smith, L.N. Performance, Reliability, Usability, and Safety of the ID-Cap System for Ingestion Event Monitoring in Healthy Volunteers: A Pilot Study. *Innov. Clin. Neurosci.* **2016**, *13*, 12–19.
43. Samokhin, A.S. Syringe Pump Created Using 3d Printing Technology and Arduino Platform. *J. Anal. Chem.* **2020**, *75*, 416–421. [CrossRef]
44. Lee, H.; Song, C.; Hong, Y.S.; Kim, M.; Cho, H.R.; Kang, T.; Shin, K.; Choi, S.H.; Hyeon, T.; Kim, D.H. Wearable/disposable sweat-based glucose monitoring device with multistage transdermal drug delivery module. *Sci. Adv.* **2017**, *3*, e1601314. [CrossRef]
45. Zhang, J.; Xu, J.; Lim, J.; Nolan, J.K.; Lee, H.; Lee, C.H. Wearable glucose monitoring and implantable drug delivery systems for diabetes management. *Adv. Healthc. Mater.* **2021**, *10*, 2100194. [CrossRef]
46. Yang, Y.-J.; Lee, H.-K.; Huang, Y.-H.; Wu, T.-F. A release-on-demand wireless CMOS drug delivery SoC based on electrothermal activation technique. In Proceedings of the 2009 IEEE International Solid-State Circuits Conference—Digest of Technical Papers, San Francisco, CA, USA, 3–7 February 2008; pp. 288–289. [CrossRef]
47. You, R.; Fu, X.; Duan, X. Acoustofluidic Based Wireless Micropump for Portable Drug Delivery Applications. In Proceedings of the 2021 43rd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), Guadalajara, Mexico, 26–30 July 2021; pp. 1276–1279. [CrossRef]

48. Jeong, J.-W.; McCall, J.G.; Zhang, Y.; Huang, Y.; Bruchas, M.R.; Rogers, J.A. Soft microfluidic neural probes for wireless drug delivery in freely behaving mice. In Proceedings of the 2015 Transducers—2015 18th International Conference on Solid-State Sensors, Actuators and Microsystems (TRANSDUCERS), Anchorage, AK, USA, 21–25 June 2015; pp. 2264–2267. [CrossRef]

49. Moussi, K.; AlDajani, M.; Kosel, J. Miniaturized Drug Delivery System for Biomedical Applications. In Proceedings of the 2019 IEEE 14th International Conference on Nano/Micro Engineered and Molecular Systems (NEMS), Bangkok, Thailand, 11–14 April 2019; pp. 97–100. [CrossRef]

50. Sarraf, E.H.; Wong, G.K.; Takahata, K. Frequency-selectable wireless actuation of hydrogel using micromachined resonant heaters toward implantable drug delivery applications. In Proceedings of the TRANSDUCERS 2009—2009 International Solid-State Sensors, Actuators and Microsystems Conference, Denver, CO, USA, 21–25 June 2009; pp. 1525–1528. [CrossRef]

51. Hamie, A.; Ghafar-Zadeh, E.; Sawan, M. An implantable micropump prototype for focal drug delivery. In Proceedings of the 2013 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Gatineau, QC, Canada, 4–5 May 2013; pp. 278–281. [CrossRef]

52. Sayeed, M.A.; Mohanty, S.P.; Kougianos, E.; Zaveri, H.P. An IoT-based Drug Delivery System for Refractory Epilepsy. In Proceedings of the 2019 IEEE International Conference on Consumer Electronics (ICCE), Yilan, Taiwan, 20–22 May 2019; pp. 1–4. [CrossRef]

53. Kotb, Y.; Hegazy, M.; Abdelrahman, K.; Nour, Z.; Al-Jebzi, M.; Ibrahim, O.; Gouda, A.; Abdel-Mottaleb, M.; Serry, M. IoT-Based Reconfigurable Micropump for Drug Delivery Applications. In Proceedings of the 2021 IEEE Sensors, Sydney, Australia, 25–27 November 2020; IEEE: Piscataway, NJ, USA, 2021; pp. 1–4. [CrossRef]

54. Khattar, R.; Srinivas, S.B.; Sharmila, A.; Balaganapathy, S. Non-Invasive IoT-Based Anaesthesia Control System. In Proceedings of the 2021 Innovations in Power and Advanced Computing Technologies (i-PACT), Kuala Lumpur, Malaysia, 27–29 November 2021; IEEE: Piscataway, NJ, USA, 2021; pp. 1–6. [CrossRef]

55. Madhav, A.; Bhamini, N.M.; Suma, H.N. An IoT Based Intravenous Drip Rate Controlling and Monitoring Device. In Proceedings of the 2021 International Conference on COMmunication Systems & NETworkS (COMSNETS), Bangalore, India, 6–8 January 2021; pp. 723–727. [CrossRef]

56. Reddy, M.A.; Pradhan, B.K.; Qureshi, D.; Pal, S.K.; Pal, K. Internet-of-Things-Enabled Dual-Channel Iontophoretic Drug Delivery System for Elderly Patient Medication Management. *J. Med. Device* **2020**, *14*, 011104. [CrossRef]

57. Indragandhi, V.; Chitra, A.; Singhania, R.; Garg, D.; Subramaniyaswamy, V. Bimodal Insulin Delivery System Using Internet of Things and Machine Learning Approach. In Proceedings of the 2021 Innovations in Power and Advanced Computing Technologies (i-PACT) 01-08, Kuala Lumpur, Malaysia, 27–29 November 2021. [CrossRef]

58. Zhang, H.; Zhu, W.; Dai, Y. A Closed-loop Remote Medical System for Real-time Diagnosis and Drug Release. In Proceedings of the IECON 2020 the 46th Annual Conference of the IEEE Industrial Electronics Society, Singapore, 18–21 October 2020; pp. 4383–4388. [CrossRef]

59. Krishna, N. IoT Enabled Therapeutic Assistance Unit for COPD Patient Drug Delivery and Management. In Proceedings of the 2022 6th International Conference on Trends in Electronics and Informatics (ICOEI), Tirunelveli, India, 28–30 April 2022; pp. 554–559. [CrossRef]

60. Farivar, F.; Jolfaei, A.; Manthouri, M.; Haghighi, M.S. Application of fuzzy learning in IoT-enabled remote healthcare monitoring and control of anesthetic depth during surgery. *Inf. Sci.* **2023**, *626*, 262–274. [CrossRef]

61. Kulkarni, M.B.; Velmurugan, K.; Prasanth, E.; Amreen, K.; Nirmal, J.; Goel, S. Smartphone enabled miniaturized temperature controller platform to synthesize NiO/CuO nanoparticles for electrochemical sensing and nanomicelles for ocular drug delivery applications. *Biomed. Microdevices* **2021**, *23*, 31. [CrossRef]

62. Sheybani, R.; Cobo, A.; Meng, E. Wireless programmable electrochemical drug delivery micropump with fully integrated electrochemical dosing sensors. *Biomed. Microdevices* **2015**, *17*, 74. [CrossRef]

63. Huang, H.; Zhao, P.; Chen, P.-Y.; Ren, Y.; Liu, X.; Ferrari, M.; Hu, Y.; Akinwande, D. RFID Tag Helix Antenna Sensors for Wireless Drug Dosage Monitoring. *IEEE J. Transl. Eng. Health Med.* **2014**, *2*, 1700108. [CrossRef]

64. Lee, J.; Cho, H.R.; Cha, G.D.; Seo, H.; Lee, S.; Park, C.-K.; Kim, J.W.; Qiao, S.; Wang, L.; Kang, D.; et al. Flexible, sticky, and biodegradable wireless device for drug delivery to brain tumors. *Nat. Commun.* **2019**, *10*, 5205. [CrossRef]

65. Lee, C.H.; Kim, H.; Harburg, D.V.; Park, G.; Ma, Y.; Pan, T.; Kim, J.S.; Lee, N.Y.; Kim, B.H.; Jang, K.-I.; et al. Biological lipid membranes for on-demand, wireless drug delivery from thin, bioresorbable electronic implants. *NPG Asia Mater.* **2015**, *7*, e227. [CrossRef]

66. Manikkath, J.; Subramony, J.A. Toward closed-loop drug delivery: Integrating wearable technologies with transdermal drug delivery systems. *Adv. Drug Deliv. Rev.* **2021**, *179*, 113997. [CrossRef]

67. Shi, Z.; Lu, Y.; Shen, S.; Xu, Y.; Shu, C.; Wu, Y.; Lv, J.; Li, X.; Yan, Z.; An, Z.; et al. Wearable battery-free theranostic dental patch for wireless intraoral sensing and drug delivery. *npj Flex. Electron.* **2022**, *6*, 49. [CrossRef]

68. Xu, G.; Lu, Y.; Cheng, C.; Li, X.; Xu, J.; Liu, Z.; Liu, J.; Liu, G.; Shi, Z.; Chen, Z.; et al. Battery-free and wireless smart wound dressing for wound infection monitoring and electrically controlled on-demand drug delivery. *Adv. Funct. Mater.* **2021**, *31*, 2100852. [CrossRef]

69. Song, H.; Luo, G.; Ji, Z.; Bo, R.; Xue, Z.; Yan, D.; Zhang, F.; Bai, K.; Liu, J.; Cheng, X.; et al. Highly-integrated, miniaturized, stretchable electronic systems based on stacked multilayer network materials. *Sci. Adv.* **2022**, *8*, eabm3785. [CrossRef]

70. Liu, J.; Liu, Z.; Li, X.; Zhu, L.; Xu, G.; Chen, Z.; Cheng, C.; Lu, Y.; Liu, Q. Wireless, battery-free and wearable device for electrically controlled drug delivery: Sodium salicylate released from bilayer polypyrrole by near-field communication on smartphone. *Biomed. Microdevices* **2020**, *22*, 53. [CrossRef]

71. Van der Schaar, P.J.; Dijksman, J.F.; Broekhuizen-de Gast, H.; Shimizu, J.; van Lelyveld, N.; Zou, H.; Iordanov, V.; Wanke, C.; Siersema, P.D. A novel ingestible electronic drug delivery and monitoring device. *Gastrointest. Endosc.* **2013**, *78*, 520–528. [CrossRef]

72. Yi, Y.; Kosel, J. A remotely operated drug delivery system with dose control. *Sens. Actuators A Phys.* **2017**, *261*, 177–183. [CrossRef]

73. Yi, Y.; Chiao, M.; Wang, B. An electrochemically actuated drug delivery device with in-situ dosage sensing. *Smart Mater. Struct.* **2021**, *30*, 055003. [CrossRef]

74. Al Ameen, M.; Liu, J.; Kwak, K. Security and privacy issues in wireless sensor networks for healthcare applications. *J. Med. Syst.* **2012**, *36*, 93–101. [CrossRef]

75. Ng, H.S.; Sim, M.L.; Tan, C.M. Security issues of wireless sensor networks in healthcare applications. *BT Technol. J.* **2006**, *24*, 138–144. [CrossRef]

76. Dai, H.-N.; Wang, Q.; Li, D.; Wong, R.C.-W. On Eavesdropping Attacks in Wireless Sensor Networks with Directional Antennas. *Int. J. Distrib. Sens. Netw.* **2013**, *9*, 760834. [CrossRef]

77. Huang, D.-W.; Liu, W.; Bi, J. Data tampering attacks diagnosis in dynamic wireless sensor networks. *Comput. Commun.* **2021**, *172*, 84–92. [CrossRef]

78. Singla, R.; Kaur, N.; Koundal, D.; Bharadwaj, A. Challenges and Developments in Secure Routing Protocols for Healthcare in WBAN: A Comparative Analysis. *Wirel. Pers. Commun.* **2022**, *122*, 1767–1806. [CrossRef]

79. Latif, R.; Abbas, H.; Assar, S. Distributed denial of service (DDoS) attack in cloud- assisted wireless body area networks: A systematic literature review. *J. Med. Syst.* **2014**, *38*, 128. [CrossRef]

80. Kumar, P.; Lee, H.-J. Security Issues in Healthcare Applications Using Wireless Medical Sensor Networks: A Survey. *Sensors* **2012**, *12*, 55–91. [CrossRef]

81. Strielkina, A.; Illiashenko, O.; Zhydenko, M.; Uzun, D. Cybersecurity of healthcare IoT-based systems: Regulation and case-oriented assessment. In Proceedings of the 2018 IEEE 9th International Conference on Dependable Systems, Services and Technologies (DESSERT), Ukraine, Kyiv, 24–27 May 2018; IEEE: Piscataway, NJ, USA, 2021; pp. 67–73.