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*Review Article*

# A Hybrid Framework of Blockchain and IoT Technology in the Pharmaceutical Industry: A Comprehensive Study

**Abidemi A. Emmanuel**,[1] **Jinmisayo A. Awokola**,[1] **Shadab Alam**,[2] **Salil Bharany**,[3] **Praise Agboola**,[1] **Mohammed Shuaib**,[2,4] **and Rafeeq Ahmed**[5]

[1]*Department of Computer Sciences, Precious Cornerstone University, Ibadan 200251, Nigeria*
[2]*College of Computer Science and IT, Jazan University, Jazan, Saudi Arabia*
[3]*Department of Computer Engineering and Technology, Guru Nanak Dev University, Amritsar, Punjab, India*
[4]*Razak Faculty of Technology and Informatics (RFTI), Universiti Teknologi Malaysia (UTM), Kuala Lumpur 54100, Malaysia*
[5]*Department of CSE, Koneru Lakshmaiah Education Foundation, Vaddeswaram, AP, India*

Correspondence should be addressed to Salil Bharany; salilbharany@gmail.com and Mohammed Shuaib; shuaib@graduate.utm.my

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The pharmaceutical company is key to having a strong healthcare system, and excellent healthcare is essential for every society and economy. However, there are significant concerns with medication safety and security as a result of fake and inferior medical items, which constitute a significant hazard and harm to consumers' health. Globally, drug counterfeiting is a severe problem that endangers the public's health as well as the health of consumers. The global business of manufacturing fake medications generates enormous annual revenue. To have a quality healthcare system, the pharmaceutical industry is of great importance and plays a vital role in medicine and pharmaceutical supplies. With emerging computer technologies like blockchain and IoT cutting across several industries and sectors and revolutionizing the world, a systematic literature review of various articles chosen from different databases was carried out in this study to analyze and evaluate application areas of this technology in the pharmaceutical industry and existing frameworks that have been proposed to solve problems faced in the pharmaceutical industry. The outcome of this review showed that the application of the blockchain and IoT hybrid framework can assist in reducing the drug counterfeit problem and provide solutions to most of the problems faced in the pharmaceutical industry. This study also proposed a framework that addressed the drawbacks of existing frameworks in the pharmaceutical industry.

## 1. Introduction

Healthcare systems worldwide continue to face challenges, which frequently result in rising costs or poorer health outcomes (morbidity and mortality) [1]. This happens for various reasons, one of which is the pharmaceutical supplies or medicines provided by the pharmaceutical industry. One of the foundational components of the healthcare system is medicine supplies [2]. Because of the huge risk that counterfeit and substandard medications represent to clients' well-being in today's health-conscious culture, drug quality and regulatory compliance have received great international attention [3]. The popularity of prescription pharmaceuticals and their widespread use, according to an article in the American Journal of Law and Medicine, "have attracted unsavory individuals interested in abusing vulnerable patients and the markets for medicines" [4]. Pharmaceutical companies invest a lot of money in the research and development (R&D) of new medications that benefit society and are recognized as safe and effective in the United States by the Federal Drug Administration (FDA), but suppliers of fake medications avoid this step and provide these medications at little cost to them; profit margins are frequently as high as 3000 per cent [5].

According to an analyst, investing $1000 in fake prescription pharmaceuticals can yield a $30,000 earning, which is ten times the profitability of heroin trafficking [6]. According to one source, selling fake sildenafil, for instance, "may be as much as 2000 times more profitable" than selling cocaine. Additionally, because detection is far more challenging, the likelihood of being discovered is substantially smaller [7]. Medical professionals relate the issue of medications that yield subpar clinical effects to patient variance, making detection challenging. Patients typically have little reason to believe they are taking fake medications. It is challenging to test for bad pharmaceuticals because the packaging is frequently thrown away, especially since the poisons may become undetected in the bloodstream within a few days. The evidence is obliterated the moment it is consumed or injected, as suggested by one case [4]. Additionally, individuals might not want to admit that they obtained medications over the internet without a prescription. As a result, there is a very low chance that a counterfeiter will be discovered [8].

Less than 1% of medicines sold in affluent nations are thought to be fake, the World Health Organization (WHO) claims. However, this percentage is only about 10% worldwide; in some developing nations, this percentage may reach up to 30%. Approximately 10–30% of the pharmaceuticals supplied in developing countries are fraudulent, which is a significant problem for the pharmaceutical industry today. Medication fraud is a global issue as well. According to estimates from the World Health Organization (WHO), up to 30% of the medicines sold in some regions of Latin America, Africa, and Asia are fake [9]. In Nigeria, 64% of antimalarial medications were discovered to be fake in 2011. An estimated 10% of medicines sold worldwide are fake [10]. The market for fake medicines is estimated to be worth $200 billion yearly, but internet sales of counterfeit medicines account for $75 billion of that figure. The main problem with these fake medications is not that they are not the real thing but that they can behave extremely different from what was previously anticipated. Because these fake medications cannot address the ailment they were intended to, they can be dangerous for individuals who take them [11]. The effectiveness of supply chain management is significantly impacted by pharmaceutical businesses' performance as key actors in the pharmaceutical supply chain. Numerous supply chain dangers are internal risks brought on by improper management of a firm's processes, people, and functions. These risks could be easily controlled by effective mitigation techniques [12]. Numerous sectors today need to overcome financial obstacles to operate efficiently and make money as a result of the current economic situation. This is particularly true in the pharmaceutical industry, where technology is continuously being created to discover new ways to treat illnesses, store medications, and work as effectively as possible [13].

Blockchain-based applications have shown promise in the development of the healthcare industry, and they have continued to prove a reliable platform for information exchange and review. Regardless, healthcare systems must be cautiously optimistic about the potential of blockchain technology and do the careful commercial and technical due diligence motivated by specific use cases [14]. The blockchain network uses cryptography to ensure that only authorized users may access all of the data. Because the blockchain is a decentralized platform with no centralized entity controlling or storing the network's occurrences, a sender who wants to make a transaction needs a blockchain P2P network [15]. Blockchain technology has essential features: immutability, distributed, decentralized, security, consensus, and unanimous. The applications of blockchain technology cut across several industries and sectors; in the pharmaceuticals firm's tamper-proof and immutability, the blockchain enables distribution network transparency and traceability process and ensures drug provenance. Also, pharmaceutical records and other prior data are kept secure and cannot be breached.

The demand for Internet of Things (IoT) devices has been progressively growing in recent years as a consequence of the expanding demand on the world market for quicker and more efficient manufacturing processes, the necessity of improving military capabilities, and the conversion of everyday objects into intelligent ones like intelligent houses, enterprises, and cities. Internet of Things gadgets have many advantages, but they also have many drawbacks. For example, they produce a large amount of data and a large amount of energy and raise trust concerns because they are centralized and under the authority of a single administrator who may alter the fundamental infrastructure or even shut it down totally. The Internet of Things (IoT) technology enables objects to gather and later share data about themselves and their surroundings. These data are sent to a central server after being captured with a device [16, 17]. This is where the integration and incorporation of blockchain technology come in IoT devices.

The blockchain architecture is, by default, decentralized. It enables IoT devices to safely and dependably exchange acquired data among themselves and transfer it to a decentralized cloud server [18]. Data privacy, security, and integrity are one of the biggest problems faced with IoT devices and can be solved using blockchain technology [19]. Figure 1 shows the pictorial representation of the world of IoT and its domains.

The pharmaceutical industry plays a critical role in having a solid healthcare system; good healthcare is vital to every country and economy. Regardless of this fact, there are main issues with drug safety and security because of falsified and substandard medical products, which pose a great threat and harm to consumers' health [20]. The pharmaceutical supply chain (PSC) involves numerous partners and intermediaries from manufacturing to consumption, which cannot ascertain transparency in today's centralized systems. Some of the global challenges faced by the pharmaceutical industry are counterfeiting drugs, data manipulation, and poor monitoring of the supply chain. Other challenges related to the management approach include lack of standardization and regulatory compliance, nonavailability of a feedback system, and loss of confidence in the medications and healthcare providers. Therefore, this review examines the overview of the existing literature on blockchain and IoT

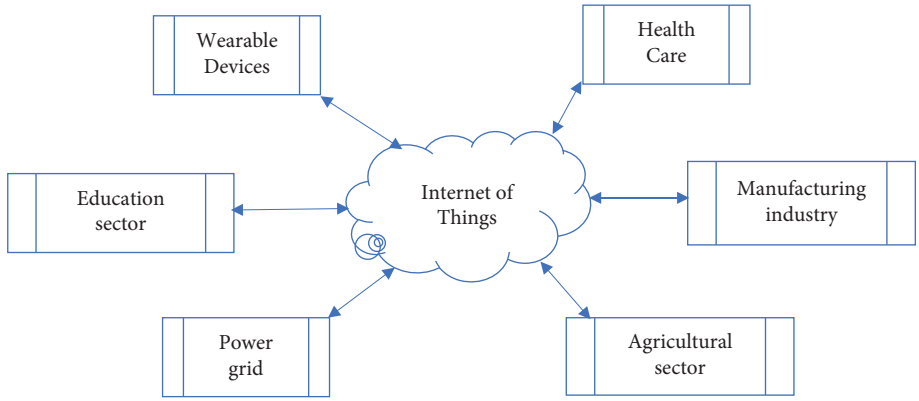


Figure 1: Internet of things technology.

in the pharmaceutical industry and proposes a novel framework with patient feedback to mitigate the problem in the existing framework as well as spur researchers to develop a more robust system for the pharmaceutical industry.

This study consists of five sections. The next section describes the literature reviews. The study reviews blockchain and IoT articles and provides a summary table for the literature showing their drawback. The methodology was described in Section 3. This section described the techniques and various databases visited and obtained articles for the systematic review. Section 4 presents the proposed framework for blockchain and IoT technologies in the pharmaceutical industry, while Section 5 concludes the study and gives a future research direction.

## 2. Related Reviews

This section entails a review of related works in the application of blockchain and IoT technology in the pharmaceutical industry.

Haq and Muselemu in the study [21] proposed the use of blockchain technology in the pharmaceutical business to combat counterfeit pharmaceuticals. The proposed model used blockchain technology as an immutable ledger and a unique identity of a hashed pharmaceutical product registered on the blockchain and labelled as a QR code to track the end user's supply chain history and provenance of pharmaceutical products. The study tends to prevent counterfeit drugs in the pharmaceutical industry but lacks the required client feedback to combat fake drug distribution. This study discussed how blockchain technology could be used to improve clinical research quality [22]. A similar model to Haq and Muselemu was proposed by Sahoo et al. [23]. The model uses blockchain technology but introduces the use of IoT to track the supply chain process from the manufacturer of a particular product to the consumer/end user. In their work, every manufacturer must be certified/licensed by a standard regulatory body and possess a unique ID to be labelled on the drug. The authors discussed healthcare and blockchain in a broad general sense [24]. However, the authors did not provide any details on blockchain in the drug production or pharmaceutical supply chain [25, 26].

Rayan and Zubair [27] proposed a medicine supply network centred on radio frequency identification (RFID) that supervises the system to safeguard the chain's security and the provision of high-quality health care. It offered a technological solution integrating blockchain, RFID, and IoT to improve the monitoring of pharmaceutical products as they travel through the pharmaceutical supply chain. The study lacks the feedback mechanism to validate the authenticity of the supply chain [28]. TrustChain is a three-layered structure for reputation administration proposed by Malik et al. [29] TrustChain was depicted as a blockchain-based supply chain application that is used to navigate trust challenges related to commodity quality.

Pandey and Dhanalakshmi [30] suggested a pharmaceutical distribution chain counterfeiting remedy. The study did an overview of different solutions and models that exist and proposed a model involving the use of smart contracts and how distributed ledger technology might assist participants in preventing counterfeit pharmaceuticals from entering the supplier base. A feasible blockchain-based anti-counterfeit pharmaceutical management system is proposed to reduce drug cloning and improve medicinal integrity. The proposed system is built on the Ethereum blockchain and the IPFS protocols to enable tamper-proof tracking [31].

Plotnikov and Kuznetsova [32] proposed using an IoT solution to provide real-time location tracking with a wireless sensor placed within the medicine packaging and blockchain as an immutable ledger for data storage. Another study offered a counterfeit prevention system that tracked medications from the manufacturer to the end user [33]. In the proposed model, manufacturers of the medication control and record all blockchain transactions. A comparison of the details of data previously stored on the blockchain with what is submitted reveals any attempted fraud, with inconsistencies revealing fake medications [34].

Subramanian et al. [35] designed and implemented a crypto pharmacy mobile application using hybrid blockchain technology to eliminate third-party presence (buy/sell) in a medicine purchase. Nem blockchain was integrated with the mobile application. Another study talked about Industry 4.0 and emerging technologies transforming the industry across every sector. The serialization process of tracking and tracing was analyzed, and it showed that it was still

susceptible to central failure, amongst several others. A better solution, NFT, was proposed that replaces all of the components of the serialization process and takes the form of distributed ledger technology through the use of blockchain [36]. A study by Gogos and Rochelle [37] evaluates the potential and drawbacks of blockchain in the pharmaceutical industry. The authors gave an overview of blockchain technology, smart contracts, and other major components of a blockchain [38].

Shashi [39] highlighted one of the most important but challenging aspects of the pharmaceutical industry temperature monitoring. Pharmaceutical items, such as medications, pharmaceuticals, vaccines, and specialty therapies, function normally when stored at a set temperature. Some of the exact and managed storage limits for different kinds of pharmaceutical items include below +25°C (controlled temperature), +2°C to +8°C (temperature-sensitive products), −20°C to −40°C (negative temperature), and −70°C (ultra-low temperature) [40]. The report also mentions that pharmaceutical goods that are not properly manufactured or delivered at the proper temperature might create difficulties when ingested. The author conducted research to identify the IoT-based digital enablers used by pharmaceutical supply chain managers to optimize the cold chain process. A model was proposed by Jammula et al. [41] using blockchain and IoT sensors to combat the problem of temperature monitoring as one of the biggest challenges faced by the pharmaceutical industry other than drug counterfeiting.

Kumari [42] identifies that fake medicines and drug counterfeiting seriously threaten the healthcare sector and society. Therefore, a blockchain-based architecture is presented to combat the danger of counterfeit drugs. The author states that the way to combat counterfeit drugs in health services and maintain and distribute health records is another major challenge. Because health records are vulnerable to confidentiality and integrity challenges, their security is a top priority. Neglecting these dangers might have serious repercussions for healthcare systems, such as patient mortality. Furthermore, Jain et al. [43] characterized the creation and distribution of counterfeit medications, particularly in poorer nations, as a critical and growing worldwide concern. Therefore, a blockchain-based solution is provided to overcome medicine counterfeiting.

Jaisimha and Kumar [44] carried out a systematic mapping study to explore blockchain's feasibility in the pharmaceutical sector's supply chain. The authors proposed the use of smart contract interaction with IoT devices to optimize the pharma supply chain. IoT is used for monitoring and regulation of critical things like temperature, weather, etc. Smart contract helps set the condition of easy transfer and purchase of the product when all the conditions are fulfilled; if not fulfilled, they do not go through. Humayun et al. [45] identified coordination flaws in the drug distribution market (DDM), coordination management, and lack of a centralized surveillance system capable of providing effective market management and providing real-time pricing, accessibility, and authentication data, as serious issues that significantly affect the global market for counterfeit drugs.

Gao et al. [46] conducted an in-depth examination of the drug companies to appreciate the advantages and disadvantages of blockchain for the industry, as well as customer impressions of blockchain application in the industry The study studies the relevant circumstances in the present healthcare industry, the understanding of blockchain technology, and evaluates the current state and issues of blockchain applications in the healthcare market as the target of research. Data security, privacy, preservation, data exchange, and interoperability are all important considerations identified as major issues and challenges faced by the pharmaceutical industry. Blockchain is a solution to break the bottleneck problems in the pharmaceutical sector [47]. Alagarsamy et al. [48] gave an overview of the application of IoT in the pharmaceutical sector. They identified the applications of IoT in facilitating and optimizing drug development, drug testing, and remote patient surveillance among other things. Table 1 summarizes the literature review.

The major drawback deduced from the list of the literature is the lack of a feedback mechanism system between the consumer and manufacturer to validate the product. This drawback causes a high rate of counterfeit drugs in the pharmaceutical supply chain. Another drawback examined from the existing work is the lack of data integrity. Therefore, developing appropriate and efficient quality systems is one of the crucial factors to consider for survival in the highly competitive pharmaceutical manufacturing industries. Creating a tailored feedback system for manufacturers and hospitals that is more grounded in real-world experiences is more dependable and sustainable than using standardized surveys [58].

## 3. Materials and Methods

For research, the study used a comprehensive analysis of qualitative information. There is significant research on IoT and blockchain in the pharmaceutical sector, but it is usually focused on a certain practice. Even though numerous articles have been published addressing the application of IoT and blockchain in the pharmaceutical business, there are still gaps in the literature in this field, which supports the current study. In this study, data from a few articles published in the recent five years (2017 to 2022) were carefully analyzed to emphasize what has been documented about the issue in both scholarly research and literature reviews.

The Methodi Ordinatio Methodology was used in this study, which describes the criteria for selecting scientific publications [48]. This approach selects articles using a modified version of the Prochnow-C, and works are rated by significance using an index called InOrdinatio.

### 3.1. Research Questions

(i) What are blockchain and IoT technology application areas in the pharmaceutical industry?

(ii) What are the drawbacks of the existing frameworks in the pharmaceutical industry?

Table 1: Summary of the literature review.

| s/n | Authors and title | Work done | Strength | Drawback |
|---|---|---|---|---|
| 1 | Haq and Muselemu [21] | Proposed a model for counterfeit medications using a mobile app to check for verification and a permission blockchain | Traceability and transparency are achieved | IoT was not incorporated into this model. Other things, like the temperature of the medical product during transportation, were not achieved |
| 2 | Benchoufi et al. and colleagues [25] | Proposed a model for protecting patient data, improving clinical research, and ensuring consent for clinical trials | Traceability and transparency are provided for clinical data | They discussed the use case of blockchain in general for healthcare, but no further explanation was given for blockchain and IoT in the pharmaceutical industry |
| 3 | Rayan and Zubair [27] | An IoT-integrated blockchain model for supply chain traceability and transparency | Transparency and real-time monitoring using blockchain and IoT technology | No in-depth explanation of the proposed model by the authors<br>No direct feedback mechanism between consumers and the manufacturer |
| 4 | Alam et al. [49] | A blockchain-based model to eliminate drug counterfeiting in the pharmaceutical industry | Transparency and traceability of the chain | (i) No explanation was given on how the consumer checks the validity of the product<br>(ii) IoT was not integrated into the model that was proposed<br>(iii) Nonavailability of a feedback system between the consumer and the manufacturer |
| 5 | Malik et al. [29] | The three-layered framework known as TrustChain uses consortium blockchain to solve trust issues with commodities and the integrity of data | Smart contract used for automation of reputation calculation | No direct feedback mechanism between the manufacturer and the consumer |
| 6 | Raj et al. [50] | Use of smart contracts and the blockchain to establish proof ownership of a product and the authenticity using the electronic product code | Automation of smart contracts in the supply chain process | No incorporation of IoT technology |
| | | | Transparency and supply chain history validity | No feedback mechanism between the manufacturer and the consumer |
| 7 | Pandey and Dhanalakshmi [30] | Smart contracts and blockchain provide solutions for drug counterfeiting | Pharmaceutical supply chain data were stored using an immutable ledger | Data integrity was not achieved. The systems depend on stakeholders storing data<br>No incorporation with IoT<br>No feedback mechanism between the manufacturer and the consumer |
| 8 | Pham et al. [31] | The anti-counterfeit medicine management system based on IPFS and ethereum network | Transparency in the proposed system using the blockchain | (i) No feedback mechanism between manufacturers and consumers |
| 9 | Makarov [34] | Evaluation of the use of smart contracts in pharmaceuticals | Application of blockchain | IoT as a solution to the problems of pharmaceuticals was not proposed<br>No feedback mechanism was suggested between manufacturers and consumers |
| 10 | Plotnikov and Kuznetsova [32] | General overview of the importance of digital technologies to fostering economy and blockchain as a major contributor to today's economy | Insights into the applications and positive effects of blockchain's implementation | No framework was proposed to solve the issue of falsified and substandard medications |
| 11 | Zakari et al. [51] | A systematic literature review on the applications of blockchain in the pharmaceutical industry, challenges, and future directions | Challenges and future directions in the adaptation and adoption of blockchain were covered by the author | No framework was proposed to solve the pharmaceutical supply chain problem |

Table 1: Continued.

| s/n | Authors and title | Work done | Strength | Drawback |
|---|---|---|---|---|
| 12 | Subramanian et al. [35] | A model to eliminate drug counterfeiting through the use of smart contracts and blockchain | Transparency and traceability | (i) No incorporation with IoT<br>(ii) No direct feedback mechanism between the manufacturer and the consumer |
| 13 | Jangir et al. [52] | Web 3 application built for pharmaceutical stakeholders that allow users to track products by querying the product ID | Traceability and transparency | No integration with IoT<br>No feedback mechanism between manufacturers and consumers |
| 14 | Chiacchio et al. [36] | Utilization of nonfungible tokens as a solution to drug counterfeiting, tracking, and tracing | Digital uniqueness of NFTS | No feedback mechanism for manufacturers and consumers |
| 15 | Gogos and Rochelle [37] | Research work on blockchain potentials in the pharmaceutical industry | The result showed that blockchain can be used for traceability and privacy, amongst several other benefits | No model was proposed for solving the pharmaceutical supply chain problem |
| 16 | Shashi [39] | Study and analysis of the cold chain system in the pharma supply chain | Use of IoT technology as an enabler | Blockchain technology was not used |
| 17 | Jammula et al. [41] | Designed a model for temperature monitoring in the pharmaceutical supply chain | The use of IoT and blockchain | The authentication of the product stops at the end user, and no feedback mechanism between the manufacturer and the consumer |
| 18 | Kumari [42] | The proposed model to curb the wide spread of counterfeit medication in the healthcare sector | The blockchain-based model ensures transparency | No explicit knowledge of the methodology was proposed |
| 19 | Jain et al. [43] | Proposed a blockchain-based solution for medicine counterfeiting | Transparency and traceability because of the blockchain | No IoT-integrated framework<br>No feedback mechanism between the manufacturer and the consumer |
| 20 | Sharma and Sikka [53] | A survey on the practical approaches to prevent drug counterfeiting using blockchain technology | Practical blockchain-based solution | No integration with IoT |
| 21 | Khubrani and Alam [54] | The supply chain management system using the IPFS and the ethereum network | Transparency and Scalability in the supply management system | An IoT framework was not integrated |
| 22 | Jaisimha and Kumar [44] | A systematic mapping study on the feasibility of blockchain in the pharma supply chain | IoT and smart contract integration for automated control of the system | No feedback mechanism in the supply chain model for the customer and the manufacturer |
| 23 | Humayun et al. [45] | A model for securing drug distribution from tampering using blockchain | Data coordination and data management using blockchain | No IoT framework was introduced |
| 24 | Gao et al. [46] | The study analyzes the future development of blockchain technology in the pharmaceutical industry and its general reception by consumers of healthcare facilities | Blockchain was found in this analysis and research as a solution to major challenges faced by the medical industry | No model was proposed on how to solve the problems faced by the medical industry<br>The study did not cover the use of IoT |
| 25 | Alagarsamy et al. [48] | IoT applications in the pharmaceutical industry | The authors identified three main applications of IoT: IoT in pharmaceutical manufacturing, IoT in drug discovery, and IoT in clinical trials | No model was proposed on how to apply IoT in the pharma industry |
| 26 | Tehrani and Jin [55] | | Wearable technology and personalized patient care through the use of IoT | The study only focused on the applications of IoT in the pharmaceutical industry, and there was no integration with blockchain technology<br>No model was proposed to address the challenges faced in the pharmaceutical industry |

Table 1: Continued.

| s/n | Authors and title | Work done | Strength | Drawback |
|---|---|---|---|---|
| 27 | Bharny et al. [56] | The anti-counterfeit model to reduce and curb the widespread drug counterfeiting and false medications | Automation of the supply chain process using IoT, transparency of supply chain history with blockchain technology, and credibility of transactions using the smart contract | No feedback mechanism between the manufacturer and the final consumer |
| 28 | Jochumsen and Chaudhuri [57] | Analysis was carried out to learn in-depth information about blockchain's potential in the pharmaceutical industry as well as its potential for supply chains and procurement | Tracking, tracing, and securing IoT were identified as ways blockchain could impact the pharmaceutical supply industry | No model was proposed to implement blockchain technology in the pharmaceutical industry |
| 29 | Lingayat et al. [58] | A blockchain model was designed to enable the security of the pharmaceutical supply chain | Transparency and immutability of the blockchain allow all records to be visible and unchanged | No feedback mechanism between the manufacturer and the consumer |
| 30 | Fekih and Lahami [59] | General overview of the knowledge of blockchain technology and its different applications in the healthcare sector | Blockchain and IoT technology applications were covered in the healthcare sector | No framework was proposed for the implementation of IoT and blockchain in the pharmaceutical industry |

(iii) What model can be used to address the drawbacks of the existing frameworks in the pharmaceutical industry?

The methodology of this system is based on a web3 application called a decentralized autonomous organization (DAO) which uses an incentive model to reward customers when they give feedback.

The incentive model is based on the use of a cryptocurrency token that powers the ecosystem of the DAO. This token has attached utility that gives it value such as governance and purchasing power of pharmaceutical products.

*3.2. Analysis of Journal Reviewed.* When the search procedure was used on the selected scientific database, 10800 articles were originally obtained. Six (0.03%) were from ScienceDirect, 721 (3.91%) from Pubmed, 120 (0.65) from Research Gate, and 9,953 (62.36%) from Google Scholar. After the preliminary title-based filtering, 9720 articles remained accessible. Each article title is examined independently using the inclusion and exclusion criteria, remaining 1270 papers. 773 publications were deleted because they had no relevance to the research topic (some were omitted because they were centered on features of IoT and blockchain that were unrelated to the pharmaceutical sector). 378 of them were chosen for further review based on their abstracts, introductions, and conclusions. 89 identical articles were removed using Endnote X8. Some articles were removed because their full contents were challenging to comprehend or their abstracts demonstrated that they had no relevance to the inquiry. Thirty publications having a Methodi Inordinatio index of more than 100 were selected for full document assessment; each was studied in its completeness, autonomously, and again using the inclusion and exclusion criteria. Table 1 contains a list of the thirty papers that were chosen as well as the data items that were retrieved.

*3.3. Public Distribution of Journals.* All of the publications selected were published between 2017 and 2022, highlighting the significance of IoT and blockchain in the pharmaceutical sector. It is stressed that the majority of the thirty articles picked ($n = 9$, 30%) were published in 2022, ($n = 5$, 16.67%) were published in 2021, ($n = 2$, 6.67%) were published in 2020, ($n = 8$, 26.67%) were published in 2019, and ($n = 5$, 16.67%) were published in 2018 while ($n = 1$, 3.33%) were published in 2017. Table 2 shows the collection of articles by year. Figure 2 displays the public distribution of the journals.

*3.4. Geographical Distribution of Journals.* Geographically, the articles were split into regions based on the primary author's address, with Asia (66.67%), Europe (16.67%), North America (13.33%), and Africa (3.33%) taking the lead. The following pie chart depicts the distribution. This breakdown demonstrated that IoT and blockchain in the pharmaceutical business and healthcare are not confined to a single region of the world but have extended around the globe, with the lowest activity coming from developing nations in Africa. Figure 3 displays the geographical distribution of the articles' sources.

Table 2: Analysis of articles by year of publication.

| Years | Articles ($n = 30$) | Percentage (%) |
|---|---|---|
| 2017 | 1 | 3.33 |
| 2018 | 5 | 16.67 |
| 2019 | 8 | 26.67 |
| 2020 | 2 | 6.67 |
| 2021 | 5 | 16.67 |
| 2022 | 9 | 30 |

*3.5. Distribution of Articles Based on Research Questions.* The publications were divided into three types based on the study's research objectives. Some of the chosen articles uniquely responded to the issues by addressing one specific aspect of blockchain and IoT in the pharmaceutical industry, while other articles mostly re-emphasized what was written in other articles. 14 of the chosen articles described the application areas of blockchain and IoT in the pharmaceutical Industry, while the remaining 16 articles either provided a framework that can be implemented or a solution to the existing problems faced by the pharmaceutical industry. Research in the existing models found that there was a lack of feedback mechanisms between manufacturers of pharmaceutical products and the final consumer. Through blockchain and IoT technology, customers can check the supply chain history of the pharmaceutical products and the temperature range at which they were transported and verify the authenticity and validity of the product based on specific requirements. Regardless of this fact, the supply chain process ends when the final consumer gets the products with no way for the manufacturers to understand critical things like business intelligence, what types of medications are to be produced based on effectiveness, general acceptability in the global market, side effects of the medications produced as they pertain to geography and demography, drug compliance with different geographies, amongst several other reasons. It also helps in increasing the reputation of the pharmaceutical company and fosters future developments as a way to deal with counterfeit medications.

To answer research question 3, a model was proposed that addresses the frameworks of the other previous models reviewed in this study (see Figure 4). This figure provides a mechanism for customer feedback in the pharmaceutical industry.

## 4. Discussion of the Model

As earlier stated, the drawback found in existing models is the lack of a feedback mechanism between manufacturers and the final consumers. Concerning that, this study proposes a model to help bridge existing frameworks' gaps and drawbacks. This model builds on existing blockchain and IoT frameworks that have been implemented and proposed to help track and trace the pharmaceutical supply chain,

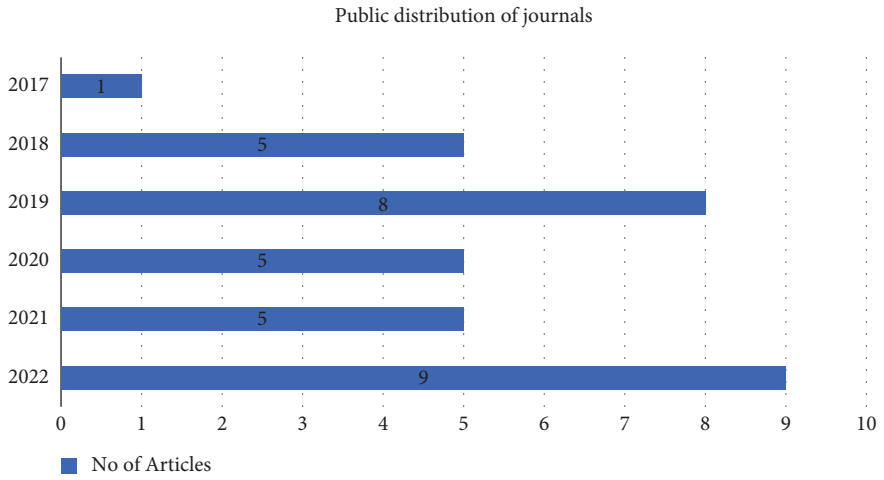


Figure 2: Public distribution of journals.

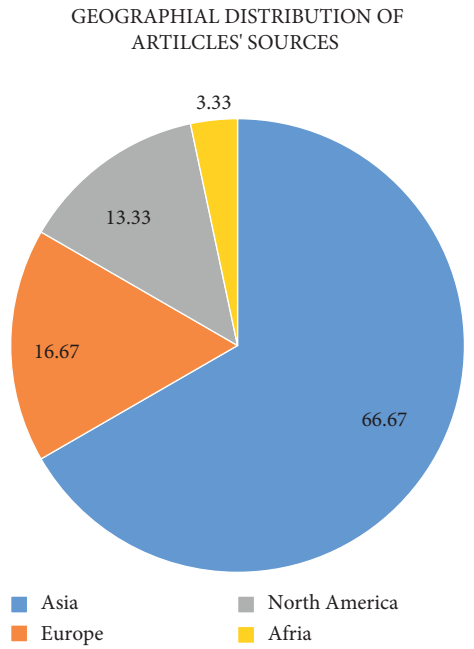


Figure 3: Geographical distribution of articles' sources.

ensure transparency, use smart contracts, proper conditions during the shipment of the products, and so much more.

For this system to be effective and widely accepted, an incentive model is attached whenever a user gives feedback to the system or manufacturer. This comes in the form of a token with several perks it offers as initially stated above. Manufacturers or producing pharmaceutical companies create a decentralized autonomous organization, and the URL is embedded in a QR code label on the product container.

The user acquires the pharmaceutical products, and after verifying the validity of the product, the user scans the QR code label on the drug using an IoT device (a smartphone, laptop, tablet, etc.). The user is then taken to the DAO and is required to access the site using a web3 service provider such as metamask or coinbase. Upon successful creation of a web3 account, the user is prompted and given full access to other features of the DAO and can give feedback on the particular product. After this is done, the system rewards the user with the crypto token of the DAO's ecosystem. Autonomous means that the user's identity is unrevealed, and the user can operate the system autonomously as no sign-up requiring personal details of the user is required, a special feature of blockchain technology and web3.

*4.1. Analysis of the Result.* Regarding the electronic databases, 0.03% (6 papers) of the articles were obtained from the science direct database. 3.91% (721 papers) were obtained from the PubMed database. 0.65% (120 papers) were obtained from the research gate database, and 62.36% (9953 papers) were obtained from the Google Scholar database.

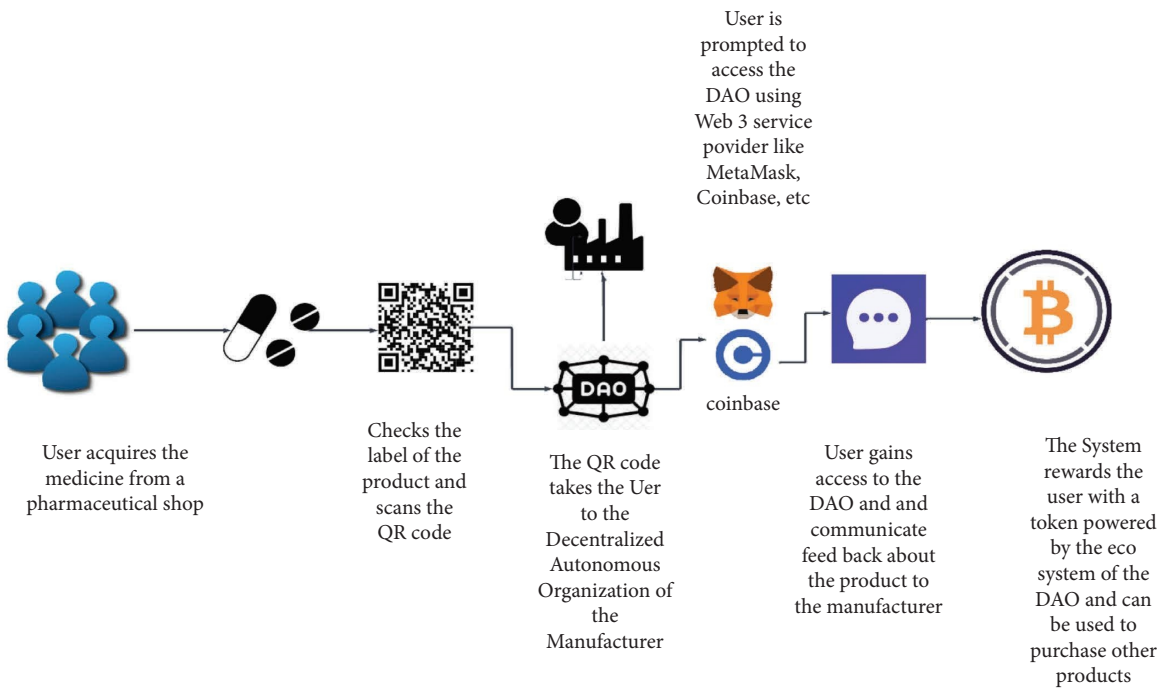


Figure 4: A hybrid framework of blockchain and IoT technology.

Table 3: Collection of the paper process.

| Database | Science direct | Pubmed | Research gate | Google scholar |
|---|---|---|---|---|
| Papers | 6 | 721 | 120 | 9953 |
| % | 0.03 | 3.91 | 0.65 | 62.36 |
| Total | | 10800 | | |

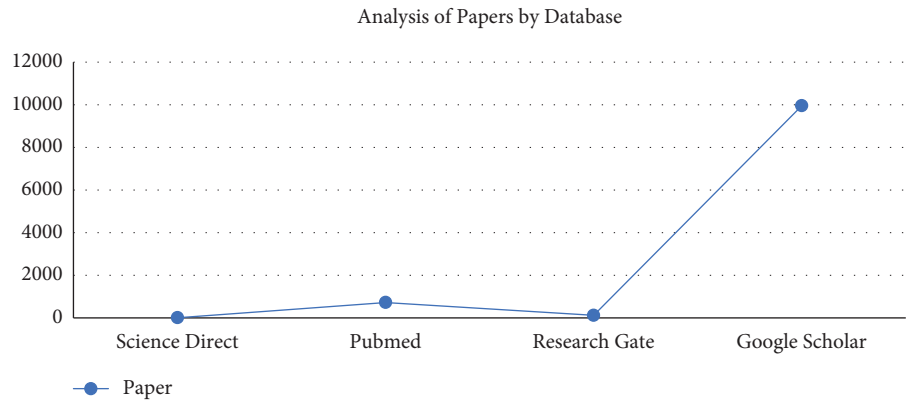


Figure 5: Public distribution of journals.

Table 3 shows the data analysis of articles extracted from various databases. Figure 5 displays the graphical representation of the paper collection. Table 4 displays the analysis of the state-of-the-art literature with the proposed study.

As shown in Table 4, only two articles offered a framework while utilizing blockchain and IoT technologies for medication delivery in the pharmaceutical sector. Many employed blockchain or IoT solely, while others proposed no framework. It was observed that the authors of references [41, 60] concentrated on bogus medication and drug counterfeit without taking into account the patient's feedback mechanism to the producer. Despite the growing relevance of blockchain and IoT, the literature has little practical research on the issue. This analysis reported that patients and drug manufacturers rarely interact with each other to obtain feedback on their products [57]. This research proposed a framework incorporating blockchain and IoT technology to allow patients to communicate with the manufacturer and provide feedback on the drugs.

Table 4: Analysis of the state-of-the-art literature.

| S/N | Author | Model | Company | Methodology | Proposed solution |
|---|---|---|---|---|---|
| 1 | Bharany et al. [56] | Yes | Pharmaceutical | Blockchain and IoT | Curb false medications |
| 2 | Jochumsen and Chaudhuri [57] | No | Pharmaceutical | IoT and blockchain | Tracking of drugs |
| 3 | Tehrani and Jin [55] | No | Pharmaceutical | IoT | Monitoring patient |
| 4 | Alagarsamy et al. [48] | No | Pharmaceutical | IoT | Drug discovery for clinical trials |
| 5 | Gao et al. [46] | No | Pharmaceutical | Blockchain | Analyzed the future of blockchain |
| 6 | Humayun et al. [45] | Yes | Pharmaceutical | Blockchain | Drug distribution |
| 7 | Jaisimha and Kumar [44] | Yes | Pharmaceutical | IoT and smart contract | Optimize pharma supply chain |
| 8 | Sharma and Sikka [53] | Yes | Pharmaceutical | Blockchain | Avoiding drug counterfeit |
| 9 | Fekih and Lahami, [59] | No | Medicine | Blockchain and IoT | General overview of the two technologies |
| 10 | Lingayat et al. [58] | Yes | Pharmaceutical | Blockchain | Security of drug distribution |
| 11 | Proposed work | Yes | Pharmaceutical | Hybrid blockchain/IoT | Provide feedback to the patient and enhance security in the drug distribution chain |

## 5. Conclusions

This study carried out a systematic literature review to understand the application areas of blockchain and IoT technology in the pharmaceutical industry and the existing frameworks that have been proposed to solve challenges relating to the pharmaceutical industry. Articles and literature were reviewed from chosen databases and analyzed. In addressing the drawbacks found in existing models of the pharma industry, a hybrid framework of blockchain and IoT was proposed for a feedback mechanism. The under-listed contributions were made to existing knowledge of this study.

(i) This study shows the research gap in blockchain and IoT technology applications in the pharmaceutical industry.

(ii) Analyzes the different methodologies and frameworks used in the pharmaceutical industry.

(iii) A model was proposed to get feedback from customers/consumers directly to manufacturers through the use of smart contracts to verify the validity and authenticity of pharmaceutical products and also help define other metrics such as effectiveness, duration of time usage, business intelligence, and drug compliance. Therefore, this study recommends the following for the future work.

(iv) A practical implementation of the proposed feedback mechanism model.

(v) Introduction of nonfungible tokens (NFTs) in the pharmaceutical industry to curb drug counterfeiting, spread awareness of diseases and symptoms, and also as a source of revenue.

The Internet of Things has impacted the pharmaceutical industry's logistics department and has created numerous opportunities. IoT integration in blockchain has significantly improved logistic operations. The Internet of Things simplifies supply chain operations and decreases the dangers that could lead to long-term disasters.

*5.1. Future Scope.* This study identifies gaps in the literature, highlights existing research activities, and proposes a research agenda for future investigations. The study's findings may help management construct a safe supply chain in medicine distribution and give a standardized feedback system in the pharmaceutical business, hence fostering decision-making processes. As a result, the findings of this study may serve as a guideline for medication manufacturers worldwide in terms of information. Because of the search criterion limitations in English, current blockchain and IoT publications published in other languages are omitted from this study. Some academic databases also are excluded. However, expanding this comprehensive study of the literature may be interesting for future research. Future studies can focus on new models, methods, and approaches for the pharmaceutical industry. The proposed framework in this study can be developed into more robust strategies for effective information dissemination and decision-making in the pharmaceutical industry.

## Data Availability

No data were used to support this study.

## Conflicts of Interest

The authors declare that there are no conflicts of interest.

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