Blockchain for Combating Pharmaceutical Drug Counterfeiting and Cold Chain Distribution

Shambhu Sarkar [a*]

[a] *Pennsylvania, USA.*

Author's contribution

The sole author designed, analysed, inteprted and prepared the manuscript.

Review Article

ABSTRACT

In recent years, pharmaceutical drug traceability systems have been developed as critical tools for improving the digital supply chain's transparency and visibility. Blockchain-based drug traceability proposes a promising solution to create a distributed shared data platform for an irreversible, trustworthy, reliable, and transparent system. This article provides a thorough analysis and summary of the current state of drug traceability distribution research on the blockchain platform by using Hyperledger febric and Hyperledger Besu methodologies. Blockchain based platform, Hyperledger Fabric and Besu meets essential needs for drug traceability such as privacy, dependability, transparency, security, authorization, authentication, and scalability. The Hyperledger Fabric blockchain platform executes drug transactions proficiently and securely in the supply chains within a distributed network of stakeholders. This fabric-enabled private, permissioned distributed network comprising various pharmaceutical stakeholder groups aids in the efficient and secure execution of medication in supply chain transactions. This study also examines the impact of blockchain technology in the healthcare system while exhibiting how some features of this disruptive technology have the potential to transform existing cold chain and drug traceability processes. Blockchain technology embraces significant benefits in the processes of pharmaceutical

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Corresponding author: E-mail: inform.shambhu@gmail.com;

drug serialization, protecting IoT devices, and ensuring temper-proof transaction sharing. Blockchain is also a potential solution to make use of IoT-enabled vehicles and warehouses for cold chain transportation by using smart sensors to capture critical temperature data. Blockchain-enabled IoT sensors in the cold chain ensure the secure transportation of drugs to pharmaceutical stakeholders in the supply chain network.

1. INTRODUCTION

The World Health Organization (WHO) categorizes fake medicines that are either masked or falsely represented as unregulated and incorrectly labeled medications whose identity and source are concealed or falsely represented on purpose as counterfeit drugs [1]. As a significant amount of these fake medications are made and spread via healthcare supply chains, they have severe detrimental side effects on the patient's life. Critical challenges like safety, security, authenticity, and traceability problems are general results of unsecure supply chain [2].

In order to address the issue of counterfeit drugs, new safe, open, and decentralized drug tracing technologies need to be developed [3,4]. Different strategies and methods have been put forth and put into practice up to this point, including mobile technology-based techniques, serial numbers and QR codes, tags with RFID, powerful computational techniques (machine learning), and serialization solutions that validate drugs at the point of sale.

Blockchain has evolved as an innovative technology that offers a system that is transparent and irreversible without the need for an authorized third party. It is a set of time-stamped, immutable blocks connected by cryptographic hashes. Each new block that has been inserted at the end of the chain contains a special code or a reference to the data that was added to a previous block [5]. Blockchain technology is mostly used to improve product safety and ensure accurate pharmaceutical product traceability. Blockchain technology solutions in supply chain and logistics have recently gained enormous acceptance as they provide an immutable and transparent way to record transactions between non-trusting stakeholders [6]. By bringing together all viable solutions and assisting in the creation of a distributed shared data platform, blockchain enables us to become more dependable, responsible, and transparent while also helping to comprehend the entire magnitude of the fake drug problem. Blockchain technology offers a decentralized, scalable solution for various applications in the pharmaceutical supply chain, eliminating the need for trusted centralized methods [7].

By using blockchain technology, we can ensure that genuine medications are delivered to a legitimate stakeholder at every transfer point and that verified and authenticated transactions remain available in Medledger. This technology facilitates collaboration between pharmaceutical stakeholders with different levels of trust, reduces obstacles in the drug supply chain, and establishes an impregnable decentralized drug tracing system [8]. Blockchain technology provides both privacy and transparency for each drug transaction in a distributed, decentralized ledger of cryptographically protected timestamped records, ensuring the authenticity of every medicine in the supply chain.

By tracing and recording transaction activity more securely and transparently through the shared ledger, the blockchain-enabled supply chain mechanism described in this article offers a reliable and proactive way to discover falsified and phony medications. Additionally, the blockchain-enabled cold chain improves and revolutionizes drug safety by monitoring temperature of medications through the sensors, proactively identifying hazards and their associated events, and acting as a shared ledger for post-transaction surveillance.

In a blockchain-enabled supply chain, it is very difficult for drug counterfeiters to supply fake drugs through illegal sources, which may increase patients' trust that their medications are real and enhance their propensity to buy. The use of blockchain applications in pharmaceutical data integration protects information from being stolen or changed, gives businesses a competitive edge, and averts resource waste by tracking the temperature of drugs at all stages of

the supply chain. The problem of drug counterfeiting in the supply chain can be mitigated by using blockchain technology for drug traceability and cold chain transportation and by supplying drugs between different companies using IoT-enabled vehicles.

2. BLOCKCHAIN ARCHITECTURAL PLATFORM FOR DIGITAL DRUG TRACEABILITY

In this article, we will discuss two blockchain-based technological architectural platforms for digital drug traceability. We will mainly focus on platforms of Hyperledger Fabric and Hyperledger Besu as the foundation of architectures because they offer a higher level of trust, decentralization, transparency, privacy, security, data integrity, deployment, modularity, and scalability than other blockchain platforms. In order to build private permissioned blockchain ecosystems where pharmaceutical stakeholders and their end-users are registered, managed, and regulated by a regulatory body, set of authorities or stakeholders, basic pharmaceutical process designs may be essential building blocks. Blockchain regulate and control the interaction among the involved parties in the drug supply chain ecosystem, chain codes are designed, coded, and implemented using sequence maps [9].

Jamil & Hang [10] presented a blockchain-based system to manage the supply chain for medicinal medications. The proposed method makes use of the proof-of-concept-based Hyperledger Fabric blockchain. The framework explains how Hyperledger Fabric blockchain works for smart hospitals, including its implementation, architecture, and performance. The healthcare ecosystem, including medical records, gets to be managed by pharmacists, nurses, patients, and doctors due to blockchain technology. Along with a permission-based blockchain system, a smart contract is created using the Solidity programming language. The Solidity programming language is used to develop a smart contract and a permission-based blockchain system. The framework reduces the problem of fake medications by relying on this blockchain- and smart contract-based approach. One of the most significant issues at the moment is the supply chain management of biologic medications, which have unique temperature and weather needs.

Bishara et al. [11] created a framework for the control of pharmaceutical drug distribution methods, quality control, risk assessment elements, and temperature monitoring. The development of this system for temperature and humidity monitoring is essential for maintaining the efficacy of biopharmaceutical drugs.

2.1 Hyperledger Fabric Architectural Platform for Pharmaceutical in the Supply Chain

Hyperledger is an open-source project that is working to create a collection of reliable frameworks, tools, and libraries enabling blockchain deployments across entire organizations [12]. When compared to other blockchain systems, Hyperledger is thought to be the most developed collaborative technology. Throughout the start of the development process until secure code is generated, Hyperledger enables the development process of blockchain-based applications in a modular manner. Hyperledger is also considered one of the most successful open-source collaborative technologies that strives to advance the advancement of cross-industry blockchain technology [13]. Along with the features shared by other blockchain technologies, Hyperledger also includes a number of distinctive designs. One of its primary objectives is to advance the project based on the distributed ledger and smart contract [14].

Hyperledger systems have nine components [15], including identity service modules, interoperability modules, consensus layers, communication layers, contract layers, data storage modules, policy service modules, encryption modules, and APIs. The consensus layer, which encompasses a number of consensus algorithms and processes, is principally in charge of determining if the transaction set that generates the block is accurate. The contract layer is in charge of carrying out business logic and reacting to requests given by the application. The sharing of accounts is made possible via the communication layer, which is in charge of transmitting each peer's information. Databases that can be plugged in are stored by the data storage module. Additionally, the encryption module supports a pluggable component that allows the exchange of numerous encryption techniques, including proxy re-encryption, homomorphic encryption, and quantum encryption. The identity service module ensures only authorized members may join the dispersed network for data exchange by adhering to strict

commercial criteria. The strategy service module is principally in charge of overseeing the implementation of strategies like consensus policies or group policies. APIs ensure clients and programs can connect to the Hyperledger system.

The fundamental responsibility of the interoperability module is information sharing, between organizations, institutions, and research facilities. The adoption of Hyperledger in healthcare information systems has grown as a result of its distinctive permission management, fine-grained access control, pluggable consensus mechanism, and improved transaction throughput. The Hyperledger Fabric platform is based on distributed ledger technology and is supported by a modular architecture that offers high levels of confidentiality, robustness, flexibility, and scalability [16]. It is an enterprise-grade distributed ledger technology (DLT) built on the blockchain that makes use of smart contracts to uphold trust between numerous stakeholders. Although Hyperledger Fabric does away with the idea of mining, it retains the beneficial characteristics of a normal cryptocurrency blockchain. It has been demonstrated that Hyperledger Fabric can handle several thousand transactions per second [17]. Hyperledger Fabric is an ideal technological process for complicated supply chain systems where numerous physical and logical processes and parties are involved. The Hyperledger Fabric for digital drug traceability architecture offers a complex design of a blockchain-based distribution process where participants in the pharmaceutical supply chain are acknowledged and their links are established using various sources to ensure the highest levels of privacy, confidentiality, and data security. Among a set of untrusted stakeholders, Hyperledger Fabric by default offers a safe and stringent crash-fault-tolerant transaction ordering to provide deterministic logs of events, protected communication, and reliable exchange of medication-related transactions. This makes it easier to develop a reliable track-and-trace provenance system to prevent the sale of fake medicines in the protected supply chain.

Uddin and Salah [16] have proposed following steps to achieve digital drug traceability with Hyperledger Fabric (Fig. 1 illustrate drug traceability in Hyperledger fabric platform).

1. Invoking a chaincode function with certain arguments in order to read and/or update the ledger through a transaction proposal.

a. According to the chaincode endorsement rules, the proposal is sent to all endorsing peers.
b. A clear endorsement policy for each chaincode that specifies which organizations and, to what extent, whose peers must sign or check each transaction for that chaincode. The client app presents this proposal to a group of peers who will endorse it in order to obtain agreement that the transaction is legitimate. This phase is called the proposal phase.
c. As a reaction to the transaction proposal submission, the client app will receive these endorsements, along with the cryptographic signatures and RW sets of the endorsing peers.
d. The client app will continue to earn endorsements until it complies with the chaincode endorsement rules, which is vital to emphasize. The ledger is not changing at this time. This phase is called the endorsement phase.
e. The client app puts together and sends the transaction proposal and responses to the ordering service as a transaction message.
f. A transaction involving RW sets, endorsing peer signatures, and channel identification is contained in this message. The decentralized Ordering Service determines and establishes the execution order of all submitted transactions per channel using a pluggable consensus system.
g. The placing of orders blocks of several drug transactions are created chronologically, with links between the hashes of subsequent blocks. This phase is called the ordering phase.
h. In the Execution phase, the Hyperledger Fabric network's leading peers get the newly generated blocks through broadcasts from the OS.
i. Then, utilizing the gossip protocol, the leading peers are in charge of communicating the blocks to other committing peers inside the organization.
j. Each organization elects its top peers, who are recognized by the Ordering Service. Peers confirm that the RW sets have not been violated since the last check and determine whether the endorsements are valid in accordance with the chaincodes' endorsement policies.
k. The transaction is designated as invalid if any endorsements are invalid or the RW sets do not reflect the present state of the world. Instead, the ledger is updated, and

all peers append the transactions to the channels' ledgers in the predetermined order, guaranteeing determinism.

l. The world state will be updated with valid transactions. While invalid ones are kept on the ledger, they do not change the global state. Finally, each peer on the network will send a notification of transaction success to the client app that submitted the transaction proposal.

2.2 Hyperledger Besu Architectural Platform for the Pharmaceutical Supply Chain

The Hyperledger Besu is an open-source Ethereum client built on Java that often powers a large number of nodes on the Ethereum mainnet. Prior to joining the Hyperledger Foundation, it was known as Pegasys Pantheon. In 2019, it changed its name to Hyperledger Besu [18]. The Hyperledger Fabric is a part of the ecosystem, which is focused on developing a suite of reliable structures, tools, and frameworks for enterprise-grade blockchain deployments [19]. Because of its adaptability, Besu gains popularity by most recent version (v22.4, May 2022).

The three types of consensus protocols supported by its most recent version are PoW (Ethash), PoS, and PoA (Clique, IBFT 2.0, QBFT). Additionally, it can be tested on test networks like Gorli, Ropsten, and Rinkeby. Several consensus methods, including Proof-of-

Work (PoW) and Proof-of-Assignment (PoA), are included in Hyperledger Besu. Besu has 8 modules, including consensus algorithms (POA, IBFT2.0, Clique, and POW), RocksDB keyvalue database, user-oriented APIs, EVM, P2P network, monitoring (allowing monitoring of nodes and performance), privacy, and permissions (Leng and Wang, 2021). It can be used to create enterprise applications that need to conduct transactions securely and quickly over a private network. Besu enables users to monitor, maintain, and operate the Ethereum network in Hyperledger. Its extensive permission frameworks were created expressly for usage in a consortium environment (Plama and Parsechi 2021). Clients are the nodes that make up an Ethereum network and run the software that executes, verifies, and builds blocks. The Ethereum Virtual Machine (EVM), which is maintained by all nodes in the network, executes transactions and smart contracts to execute the network's state from each block. A smart contract is a collection of data and code that is stored at a specific address on the Ethereum blockchain, defines its state of activities, and automatically enforces the pre-set rules to carry out the activities as planned [18]. Due to its adaptability, enhanced privacy, and fast performance, Hyperledger Besu has recently attracted a lot of attention in the development of corporate decentralized apps [20,21]. The Ethereum virtual machines (EVMs), Orion nodes, and Ether Sign are the three core elements of the Hyperledger Besu architecture.
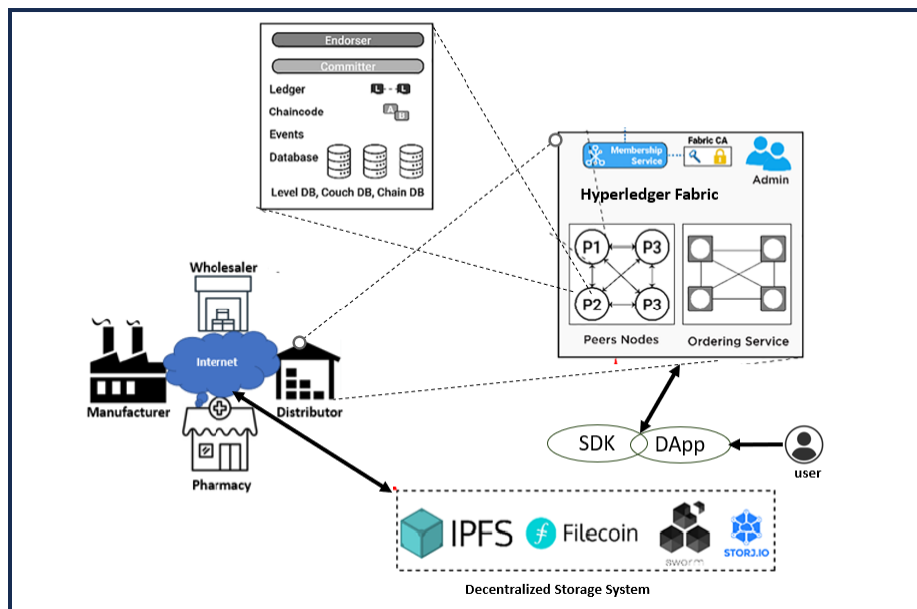

Fig. 1. Hyperledger fabric architectural platform

Hyperledger Besu allows the secure storage of data related to the execution of private and public drug transactions, which is required to implement efficient drug traceability between the supply chain stakeholders. Despite having a public blockchain as a foundation, privacy and permission features are crucial. A permissioned private ledger for the pharmaceutical supply chain establishes a specific organization and their nodes with their peer network accounts in Hyperledger Besu. It uses a public key cryptosystem, in which nodes issue a private and public key pair to authenticate transactions in the network [22]. The storage of data relevant to the execution of both private and public pharmaceutical transactions is supported by Hyperledger Besu, which can be used to provide drug traceability amongst various parties along the supply chain. In the blockchain-enabled pharmaceutical cold chain, every authorized trade partner will have a unique hash ID, which will be used for temperature monitoring transactions [23]. This will guarantee that pharmaceutical drugs will reach the supply chain partners in their original potency as they will reach the required temperature with the help of IoT sensors installed in the vehicle.

3. PHARMACEUTICAL COLD CHAIN IN BLOCKCHAIN ENABLED SUPPLY CHAIN

The pharmaceutical cold chain is a system of regulations and practices that guarantees the safe delivery and storage of medications to healthcare service providers at all levels, from the federal to the local. Refrigeration equipment that is connected to the cold chain enables medications to be stored at appropriate temperatures to preserve their potency. Advanced biologic therapeutics, including monoclonal antibodies and vaccines, cellular and gene therapies, and some treatments for rare diseases fall under the category of cold-chain pharmaceuticals, which require a secure infrastructure to maintain a specific temperature range during transport from the manufacturer to the patient. Based on its direct impacts on public health and people's lives, the pharmaceutical cold chain in particular is a complex and sensitive chain that needs to be controlled correctly.

Pharmaceutical drugs require a specific environment to store, transport, and distribute in the supply chain [24]. These requirements bring cold chain management (CCM) into supply chain distribution [25]. A cold supply chain is necessary to control environmental changes for products that are sensitive to temperature, humidity, and illumination intensity, such as pharmaceutical drugs, chilled food, frozen food, and short-lived products.

Pharmaceutical cold chain distribution must pass through several logistics networks, and each network uses a unique set of transportation and information systems. Mainly, pharmaceutical product quality is decreased by environmental changes and variations, which have an adverse impact on consumer health [26]. The upper limit of temperature for most medications is 25°C, though in exceptional circumstances it might be increased to 30°C. The category of refrigerated medications must be stored between 2 and 8 degrees Celsius. The permanent maintenance of temperature values within the aforementioned limits during all transit and storage procedures is referred to as the cold chain [27]. Drugs that are inactive or useless can be discarded by medical experts or patients based on their ability to examine the temperature conditions and validity of medications. When an appropriate drug is identified, that medication needs to be closely observed because the helpful constituents are temperature-sensitive and the medication needs to be valid.

3.1 Benefits of Blockchain Use in Pharmaceutical Cold Chain Processes

The first direct benefit of blockchain is that it may offer a solution for identity management [28]. Blockchain technology in the cold chain can play a vital role in identifying who is doing what task in the supply chain. It can also identify the act, date, and time of the task performed. Determining what actions are being performed and by whom, when, and where are the overall benefits of using blockchain in pharmaceutical cold chains [29]. The input tracking data in the blockchain ledger is immutable. Some critical medicines require a temperature-controlled environment or have a short-dated batch expiration to maintain their quality and potency. On the other hand, the stakeholders need to monitor these shipments if they are delivered to the wrong places or delayed in a location for a longer duration.

In a blockchain-enabled environment, the stakeholders in the supply chain will have greater visibility to measure accurate product quality during transportation. This system needs to be

designed to keep track of the naturally occurring temperature zones and any potential important control points. It entails not only the fulfilment of a list of specific requirements by the selection of suitable warehouses, utilities, transportation methods, and routes, but also the development and implementation of a secure and effective measurement data monitoring system, as well as the accurate and reliable climate monitoring of various existing temperature areas. Fig. 2 shows that the stakeholders in the pharmaceutical supply chain can track their shipment and its progress.

By adopting blockchain technology, efficiency can be improved and expenses decreased by getting rid of middlemen and auditors. Reducing warehousing and shipping costs as well as increasing the market competitiveness of cold chain firms can be achieved in large part through intelligent cold chain product demand forecasting [30]. On a nearly real-time basis, vendors and suppliers can track their own checks and balances.

3.2 Monitoring of Cold Chain Based on Blockchain and IoT in Pharmaceutical Distribution

The logistics and medical supply chain industries are responsible for delivering heat-sensitive medications, such as vaccines and insulin, to patients, pharmacies, and hospitals. The reliable traceability of pharmaceutical products throughout their entire life cycle must be ensured by pharmaceutical cold chain monitoring. A smart transportation box that regulates temperature and logs all changes into a pre-programmed sensor is needed to carry these medications over

thousands of kilo-meters. Blockchain can be utilized to address the issue of data reliability in the process of monitoring the cold chain for pharmaceuticals because of its decentralization and non-tampering features.

Blockchain technology is capable of storing all sensor data secure and unchangeable [30] introduces a cloud storage module that is responsible for data storage. In this process, data can't be faked if it is signed with a private key before being stored. It can obtain the pertinent data and confirm its integrity by logging the data address and hash value in the blockchain. Systems utilizing information and communication technology (ICT) are used to manage changes in the environment. Using a data-driven methodology, these tools assist managers in creating various models of supply chain systems [31]. A distributed database known as a distributed ledger or blockchain is made up of a data model that represents the ledger's current state, a language for handling transactions and changing the state of the ledger, and a protocol that is used to reach agreement among network nodes on which transactions should be accepted.

By utilizing distributed ledger technology in the pharmaceutical supply chain, it is feasible to enhance the cold chain's operational procedures, save monitoring data almost instantly, spot issues as they arise, and act swiftly to address them. Anyone linked to the blockchain system has access to all the crucial details regarding how pharmaceuticals are introduced into and transferred through the supply chain. Data can be utilized for compliance and auditing procedures because it cannot be modified after it
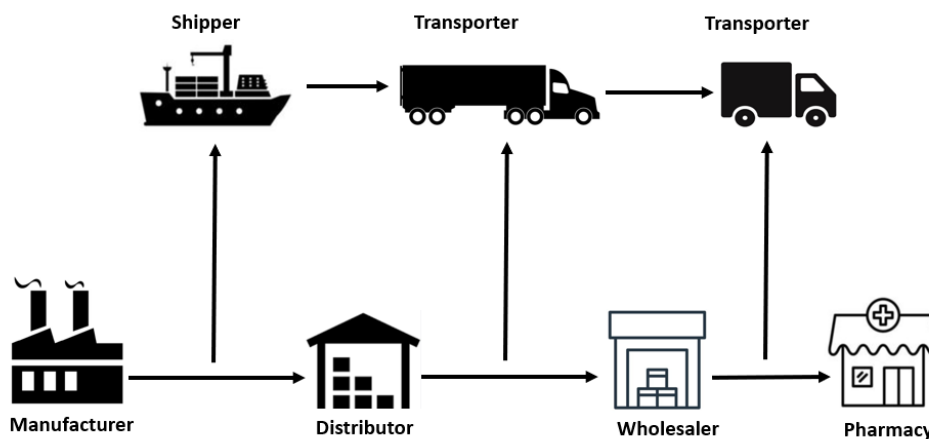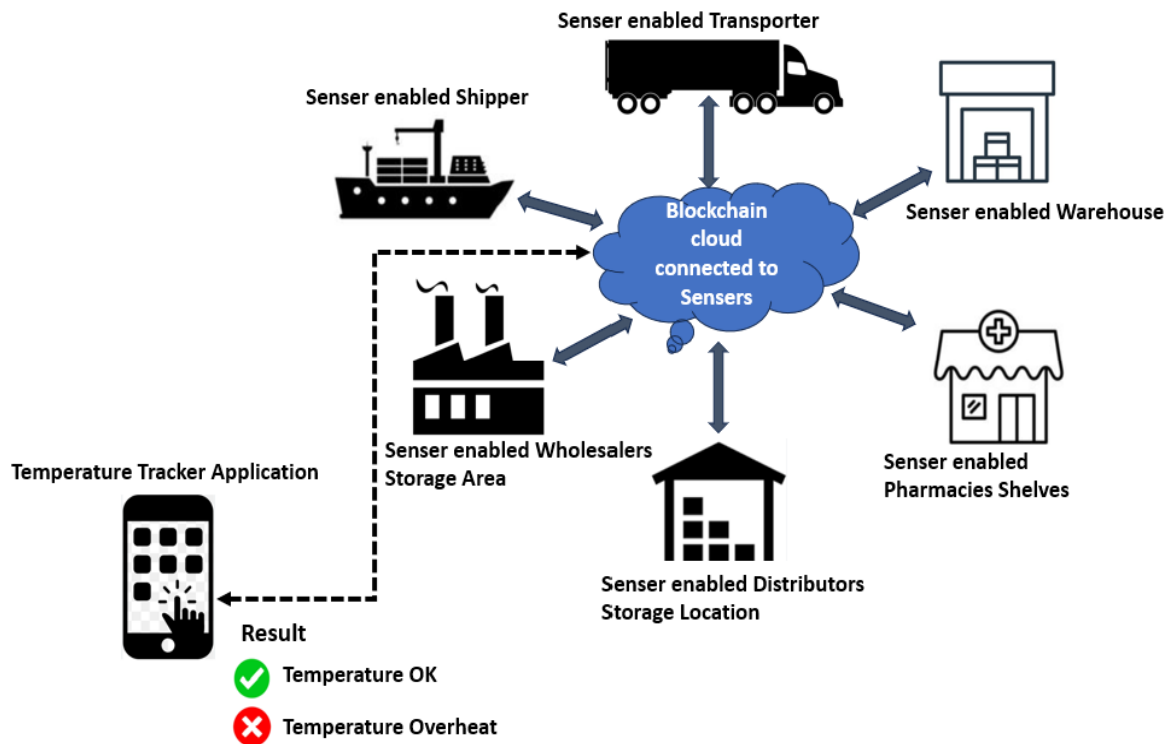

Fig. 2. Pharmaceutical cold chain from manufacturer to pharmacy

Fig. 3. Temperature monitoring in pharmaceutical supply chain

has been saved on the blockchain. Internet of Things (IoT) sensors are used to collect data about the environment, and blockchain technologies in the supply chain give a new approach to creating a trusted environment for such devices without the need to set up a sophisticated and expensive IT infrastructure. To reduce the processing time of intermediate steps in the supply chain, some procedures, such as real-time temperature tracking at every port of entry, docking, and alerting on crossing temperature thresholds, can be automated to achieve the highest efficiency. Fig. 3 illustrates how the sensor connected to IoT devices can collect temperature data inside the logistic containers while drugs are in transit in the supply chain.

4. LIMITATIONS AND CHALLENGES OF BLOCKCHAIN

In the study, we observed that the pace of research in the blockchain for pharmaceutical drug counterfeiting is relatively modest compared to other areas of research. Adoption of blockchain technology in pharmaceutical drug traceability faces challenges such as technical agility, interoperability, resistance from trade partners, uniform data practices, regulatory limitations, readiness for transparency, and

challenges from other emerging technologies. IoT networks are very large and size of IoT networks will grow manifold as more organizations and entities use them. The network's scalability is one of the most well-known limitations of blockchain technology. Since the beginning of the blockchain community, scalability has been regarded as one of the most important issues with the blockchain technology. Due to restrictions on block size, many blockchains take a long time to process transactions before they are recorded into the chain of previously confirmed blocks. As a result, block time rapidly increases, decreasing overall system performance. If every transaction is recorded on the chain, the ledger will eventually grow to be very huge [9].

It can be difficult to integrate IoT devices with blockchain technology because IoT devices produce a lot of data, and the magnitude of IoT data would grow rapidly, making the processing of high volumes of data in the blockchain complicated. Similarly, blockchains have a slow throughput or transaction execution rate, so they are unable to handle large databases. These transactions are processed through a number of phases, such as creating a transaction with high security, mining it, validating it, and storing it among numerous parties. These steps together

consume considerable computing power [32]. Furthermore, processing these high-volume transactions on the blockchain may also result in slower speeds or higher latency.

Many consensus techniques are available for blockchain that handle high throughput; however, they demand very high network usage and powerful computational hardware to perform transaction validation. Raft consensus methods, which offer great throughput but are only appropriate for a small number of network users, Raft's efficiency and throughput decline as the number of nodes in the network grows because of the network's poor scalability. Numerous well-known standard algorithms, such as AES, cannot meet the fundamental needs of restricted hardware.

Blockchain infrastructure requires vital management, networking firewalls, audits, and other technical security considerations. In the current environment, industries are looking for cost-effective blockchain platforms that include low-cost hardware implementation, low power consumption, and high-speed internet with low latency. Particularly in the cold chain, the security of sensor devices using lightweight digital signature methods is a significant problem that needs to be addressed. A digital signature can be crucial in determining whether the sensor data is coming from a trustworthy source. There is always some discrepancy between the on-chain tokens and the underlying off-chain assets. The implementation of blockchain requires significant changes to be made to the existing systems, which would require a lot of time, careful planning, money, improvement in existing network infrastructure, and human skills.

As of now, blockchain implementation in developed countries such as the United States and Europe is feasible due to their technical infrastructure and ability to invest in emerging technologies. On the other hand, implementing blockchain in developing countries for pharmaceutical drug traceability and cold chain is difficult due to their economic conditions. Unless all the stakeholders in the global supply chain participate in a blockchain-enabled interoperable network, we cannot fully benefit from blockchain technology for combating drug counterfeiting.

5. CONCLUSION

Blockchain technology, with an emphasis on cost and safety, may assist pharmaceutical cold chains and combat drug counterfeiting on a blockchain platform. This paper explains how a blockchain-based system can be potentially effective for drug traceability and detection of fake medicines in the supply chain. Blockchain platforms can integrate with cloud storage modules to solve data storage problems. In order to efficiently track drug fraud, blockchain is capable of combining large-scale heterogeneous data produced from numerous sources. Blockchain makes it easier to track down anything at any time, that include monitoring temperature in pharmaceutical supply chain, even medical supplies and prescriptions. The authorized parties can track the data at any moment in every transaction recorded to the blockchain platform in the drug supply chain. One of the key potentials that would be able to revolutionize the healthcare industry with the integration of blockchain is decentralized storage, which maintains different versions of the data in multiple locations based on authorized stake-holders permission.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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