Review Article

Blockchain for Combating Pharmaceutical Drug Counterfeiting and Cold Chain Distribution

Abstract; *The purpose of this paper is to explain the essence of the blockchain-enabled supply chain for combating drug counterfeiting. Counterfeit drugs pose a very serious threat to the supply chain in the pharmaceutical industry. In order to hide the drug's validity, criminals or counterfeiters make fake pharmaceutical drugs by imitating the identical labels and packaging. These counterfeit medications may be harmful to the patient's health since they either lack potency or have insufficient ingredients. The growth of online and Internet-based pharmacies has complicated and increased the complexity of the safety and security of the drug supply chain process. This article provides a thorough analysis and summary of the current state of drug traceability and cold chain distribution research on the blockchain platform. According to recent studies, blockchain technology offers fresh perspectives on how to improve the healthcare information system. In general, Blockchain technology embraces significant benefits in the processes of pharmaceutical drug serialization, protecting IoT devices, and ensuring temper-proof transaction sharing. This article explains the essence of a novel blockchain-enabled supply chain by leveraging the Hyperledger Fabric and Besu blockchain platforms using coincodes. The Hyperledger Fabric blockchain platform executes drug transactions proficiently and securely in the supply chain 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.*

Keywords: Drug Traceability, Pharmaceutical Serialization, Drug Counterfeit, Supply chain, Blockchain, Track and Trace System.

1. Introduction

Since the early 19th century, counterfeit medicines have been a major global challenge for governments and regulatory agencies. 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 either concealed or falsely represented on purpose as counterfeit drugs (O'Hagan and Garlington, 2018). These medications—which may be both generic and branded—contain deceptive information, including inaccurate labeling, inadequate, and erroneous amounts of ingredient(s), and, more significantly, improper packaging (Mackey and Liang, 2011). According to estimates from the WHO, one in ten medicines available on the market in low- to middle-income countries are either subpar or fake. Contrarily, between 1 and 2 percent of all medications produced and used in western markets are fake (Daniela Bagozzi, 2017). More than 1500 examples of counterfeit drug mishaps in closed pharmaceutical supply chains have affected 69 different countries (Mackey et al., 2015). Additionally, according to WHO estimates, millions of people worldwide may be either directly or indirectly impacted by these fake medications, which have grown into a multi-billion-dollar business (Clark, 2015). Furthermore, the world's market for fake medications is increasing, with the pharmaceutical industry raking in more than 200 billion Euros annually. 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 (Venhuis et al., 2015). Manufacturers of fraudulent medicines rely heavily on the gray drug markets as they use contaminated, inadequately maintained, fabricated materials and supply them from illegal sources. The growth of online pharmacies and the increasing supply of fake medicine through illegal routes both significantly and unquestionably contribute to the spread of fake medications. Typically, participants in the pharmaceutical supply chain, like secondary distributors, wholesalers, traders, and resellers, are heavily affected by these sources (Rosenthal, 2012). The bulk of commercial organizations rely on centralized third-party solutions to manage such complicated supply chains since they lack an integrated perspective of the entire system. Critical challenges like safety, security, authenticity, and traceability problems are general results of it (Azzi et al., 2019). In order to combat the shadowy underbelly of the world's largest drug fraud market, the complex structure of the pharmaceutical supply chain with its wide range of stakeholders is receiving significant attention from international pharmaceutical regulatory agencies, world health organizations, and the research community. Governments and pharmaceutical regulatory bodies all around the world now have a mission to develop an effective and efficient traceability system (Dai et al., 2015). The global healthcare sector struggles to put the newest technologically enabled frameworks and solutions to work against medication traceability problems, such as secure network infrastructures and reliable identity and authentication systems for drug supply chain participants. In order to address the issue of counterfeit drugs, new safe, open, and decentralized drug tracing technologies need to be developed (Hastig and Sodhi, 2020; Archa, 2018). 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), serialization, and m- and e-pedigree solutions that validate drugs at the point of sale. In order to trace movements and transactions across the pharmaceutical supply chain, e-pedigree and m-pedigree solutions offer drug-related traceability and tracking systems. Drug transactions are documented at each stage of trade, sale, or acquisition of products to establish the authenticity of pharmaceutical drugs. These approaches don't work together, and they don't do anything to stop fake medicines from being sold, ultimately endangering patient lives (Huang et al., 2018). 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 (Queiroz et al., 2019). 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 (Khan and Salah, 2018). 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 parties with different levels of trust, reduces obstacles in the drug supply chain, and establishes an impregnable decentralized drug tracing system (Roman-Belmonte et al., 2018). Blockchain technology provides both privacy and transparency for each asset 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 supply chain improves and revolutionizes drug safety by stepping up the monitoring of fake medications, proactively identifying counterfeit hazards and their associated characteristics, and acting as a shared ledger for post-transaction surveillance.

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 regulating bodies, set of authorities or stakeholders, these designs may be essential building blocks. In order to 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 (Uddin, 2021).

Jamil & Hang (2019) 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. (2006) 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. (Ramirez, 2020) 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 (Aggarwal, 2020). 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 (Antal, 2021). Hyperledger systems have nine components (Blummer, 2018), 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, including 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 (Uddin and Salah 2021). 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 (Gorenflo, 2019). 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 (Uddin and Salah, 2021) have proposed following steps to achieve digital drug traceability with Hyperledger Fabric.

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

I. According to the chaincode endorsement rules, the proposal is sent to all endorsing peers.

II. 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.

III. 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.

IV. 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.

V. The client app puts together and sends the transaction proposal and responses to the ordering service as a transaction message.

VI. 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.

VII. 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.

VIII. In the Execution phase, the Hyperledger Fabric network's leading peers get the newly generated blocks through broadcasts from the OS.

IX. Then, utilizing the gossip protocol, the leading peers are in charge of communicating the blocks to other committing peers inside the organization.

X. 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.

XI. 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.

XII. 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.

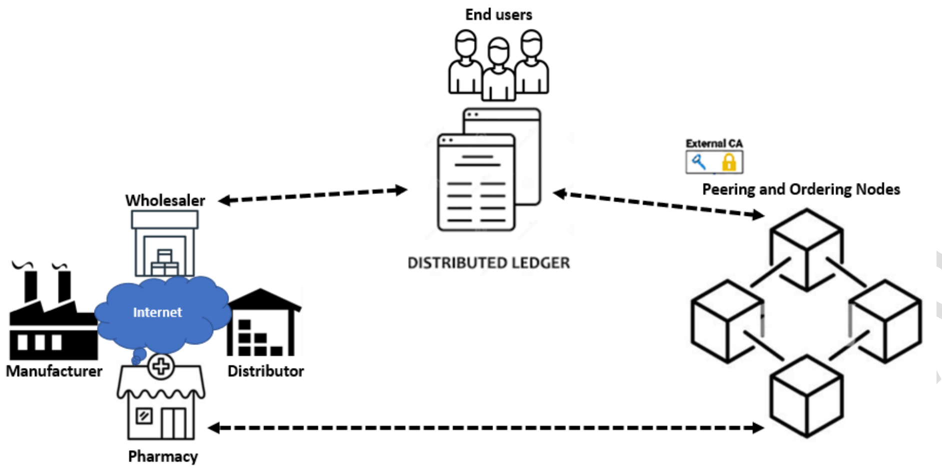

Figure 1. Hyperledger Fabric Architectural Platform

2.2 Hyperledger Besu architectural platform for the pharmaceutical supply chain

The Hyperledger Besu drug traceability architecture offers a fully compatible open-source distributed ledger solution for businesses looking for blockchain architectures. Prior to joining the Hyperledger Foundation, it was known as Pegasys Pantheon. In 2019, it changed its name to Hyperledger Besu. It is an open-source Ethereum client built on Java that often powers a large number of nodes on the Ethereum mainnet. The three types of consensus protocols supported by its most recent version (v22.4, May 2022) 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 (Fan and Khazaei, 2022). 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 (Abdella and Tari, 2021; Pradhan and Singh, 2021). The Ethereum virtual machines (EVMs), Orion nodes, and EtherSign are the three core elements of the Hyperledger Besu architecture. Despite having a public blockchain as a foundation, privacy and authorization features are crucial. (Tahmasbzadeh & Kabirirad, 2023) 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.

3. Pharmaceutical Cold Chain in Blockchain Enabled Supply Chain

In general, temperature-controlled supply chains are known as cold chains. 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. The first direct benefit of blockchain is that it may offer a solution for identity management (Alam, 2016). 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. In particular, adopting blockchain in the supply chain can benefit the pharmaceutical cold chain in terms of digital traceability, drug serialization, data security, transparency, and integrity. Pharmaceutical drugs require a specific environment to store, transport, and distribute in the supply chain (Jochumsen and Chaudhuri, 2018). These requirements bring cold chain management (CCM) into supply chain distribution (Shih and Wang 2016). 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 (Tsang et al., 2018). 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 (Hulea and Miron, 2018). 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. Determining what actions are being performed and by whom, when, and where are the overall benefits of using blockchain in pharmaceutical cold chains (Kshetri, 2018). 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. 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 (Zang and Liu, 2021). On a nearly real-time basis, vendors and suppliers can track their own checks and balances. On the other side, it is very difficult for drug counterfeiters to supply fake drugs in the supply chain through illegal sources. In this approach, blockchain-based solutions may increase patients' trust that their medications are real and increase 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.

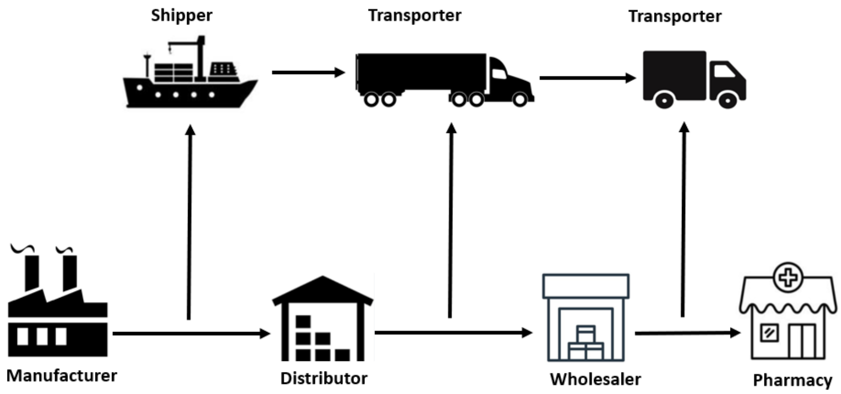

Figure 2. Pharmaceutical cold chain from manufacturer to pharmacy.

3.1 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 kilometers. 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 and is unchangeable. P. Zhang (Zang and Liu, 2021) 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. We 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 (Madhwal and Panfilov, 2017). 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 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. The sensor connected to IoT devices can collect temperature data inside the logistic containers while drugs are in transit in the supply chain.

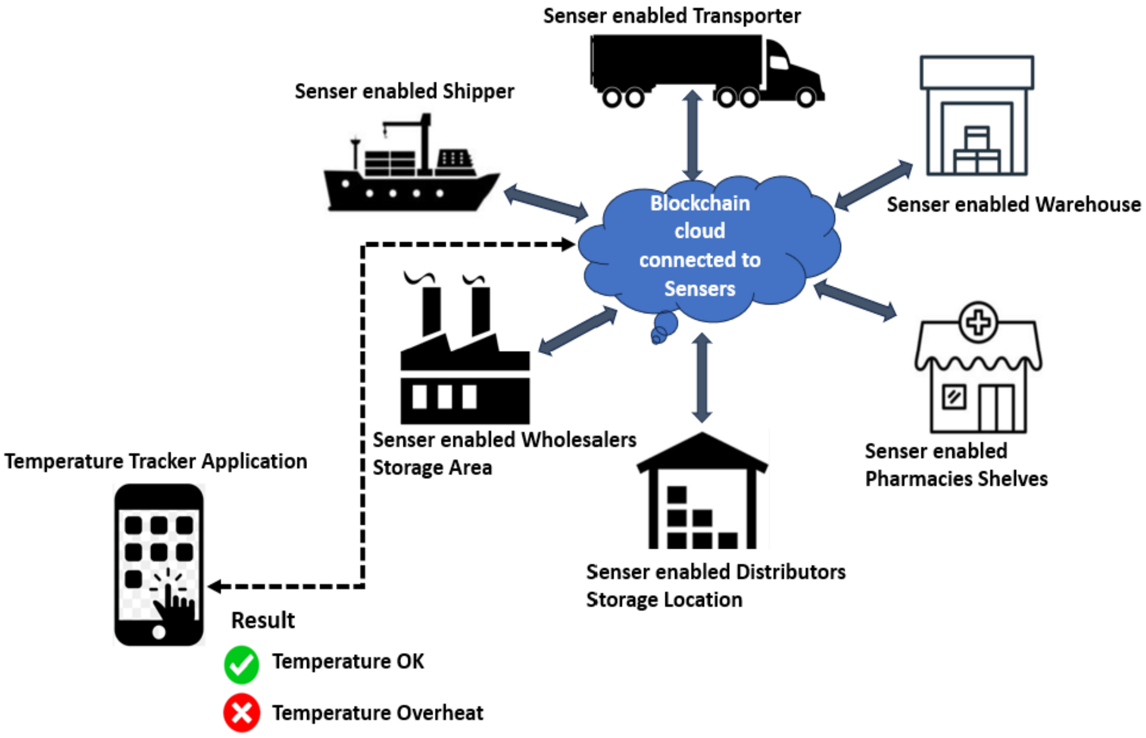

Figure 3. Temperature Monitoring in Pharmaceutical Supply Chain.

To reduce the processing time of intermediate steps in the supply chain, some procedures can be automated to achieve the highest efficiency.

3. Limitations and challenges of Blockchain

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 technology. It can be difficult to integrate IoT devices with blockchain technology. IoT devices produce a lot of data; on the other hand, blockchains have a slow throughput or transaction execution rate, so they are unable to handle large databases. Many consensus techniques are available for blockchain that handle high throughput; however, they demand very high network usage. 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.

This includes the requirement for low-cost hardware implementation, low power consumption, and 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 cryptocurrency 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, and human skills.

4. Conclusion

This paper articulates the management of pharmaceutical cold chains and drug traceability on a blockchain platform, focusing on safety and cost. This paper also explains how blockchain-based system for drug traceability can detection of fake medicines in the supply chain. Blockchain technology is mostly used to improve product safety and ensure accurate pharmaceutical product traceability. The primary advantage of the Blockchain system is the fusion of cutting-edge technologies that enables immutable, reliable distributed storage for drug tracking. Blockchain platforms can integrate with cloud storage modules to solve data storage problems. In order to efficiently track prescriptions and stop 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, 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 (Gordon, 2018)

REFERENCE

[1] O'Hagan, A., & Garlington, A. (2018). Counterfeit drugs and the online pharmaceutical trade, a threat to public safety. Forensic Research & Criminology International Journal, 6(3), 151-158.

[2] Mackey, T. K., & Liang, B. A. (2011). The global counterfeit drug trade: patient safety and public health risks. Journal of pharmaceutical sciences, 100(11), 4571-4579.

[3] Bagozzi, D. CL 1 in 10 Medical Products in Developing Countries Is Substandard or Falsified. 2017.

[4] Mackey, T. K., Liang, B. A., York, P., & Kubic, T. (2015). Counterfeit drug penetration into global legitimate medicine supply chains: a global assessment. The American journal of tropical medicine and hygiene, 92(Suppl 6), 59.

[5] Clark, F. (2015). Rise in online pharmacies sees counterfeit drugs go global. The Lancet, 386(10001), 1327-1328.

[6] Cohen, P. A., Travis, J. C., & Venhuis, B. J. (2015). A synthetic stimulant never tested in humans, 1, 3- dimethylbutylamine (DMBA), is identified in multiple dietary supplements. Drug testing and analysis, 7(1), 83-87.

[7] Rosenthal, E. T. (2012). The “gray market” raises concerns about cost, safety, and ethics.

[8] Azzi, R., Chamoun, R. K., & Sokhn, M. (2019). The power of a blockchain-based supply chain. Computers & industrial engineering, 135, 582-592.

[9] Dai, H., Ge, L., & Zhou, W. (2015). A design method for supply chain traceability systems with aligned interests. International Journal of Production Economics, 170, 14-24.

[11] Hastig, G. M., & Sodhi, M. S. (2020). Blockchain for supply chain traceability: Business requirements and critical success factors. Production and Operations Management, 29(4), 935-954.

[12] Archa, Alangot, B., & Achuthan, K. (2018). Trace and track: Enhanced pharma supply chain infrastructure to prevent fraud. In Ubiquitous Communications and Network Computing: First International Conference, UBICNET 2017, Bangalore, India, August 3-5, 2017, Proceedings 1 (pp. 189-195). Springer International Publishing.

[13] Huang, Y., Wu, J., & Long, C. (2018, July). Drugledger: A practical blockchain system for drug traceability and regulation. In 2018 IEEE international conference on internet of things (iThings) and IEEE green computing and communications (GreenCom) and IEEE cyber, physical and social computing (CPSCom) and IEEE Smart Data (SmartData) (pp. 1137-1144). IEEE.

[14] Queiroz, M. M., & Wamba, S. F. (2019). Blockchain adoption challenges in supply chain: An empirical investigation of the main drivers in India and the USA. International Journal of Information Management, 46, 70-82.

[15] Khan, M. A., & Salah, K. (2018). IoT security: Review, blockchain solutions, and open challenges. Future generation computer systems, 82, 395-411.

[16] Roman-Belmonte, J. M., De la Corte-Rodriguez, H., & Rodriguez-Merchan, E. C. (2018). How blockchain technology can change medicine. Postgraduate medicine, 130(4), 420-427.

[17] Uddin, M. (2021). Blockchain Medledger: Hyperledger fabric enabled drug traceability system for counterfeit drugs in pharmaceutical industry. International Journal of Pharmaceutics, 597, 120235.

[18] Jamil, F., Hang, L., Kim, K., & Kim, D. (2019). A novel medical blockchain model for drug supply chain integrity management in a smart hospital. Electronics, 8(5), 505.

[19] Bishara, R.H. Cold chain management—An essential component of the global pharmaceutical supply chain. Am. Pharm. Rev. 2006, 9, 105–109.

[20] Aggarwal, S., & Kumar, N. (2020). Hyperledger: An industrial approach to blockchain.

In Hyperledger (pp. 2-21). Elsevier.

[21] Antal, C., Cioara, T., Antal, M. and Anghel, I. (2021). Blockchain platform for COVID-19 vaccine supply management. IEEE Open Journal of the Computer Society, pp.1–1.

[22] Ramirez Lopez, L.J. and Beltrán Álvarez, N. (2020). Blockchain application in the distribution chain of the COVID-19 vaccine: a designing understudy.

[23] T. Blummer, M. Sean, C. Cachin, An introduction to Hyperledger. Linux Found, 2018. [Online]. Available:https://www.Hyperledger.org/wpcontent/uploads/2018/08/HL_Whitepaper_IntroductiontoHyperledger.pdf

[24] Uddin, M., Salah, K., Jayaraman, R., Pesic, S., & Ellahham, S. (2021). Blockchain for drug traceability: Architectures and open challenges. Health informatics journal, 27(2), 14604582211011228.

[25] Gorenflo, C., Lee, S., Golab, L., & Keshav, S. (2020). FastFabric: Scaling hyperledger fabric to 20 000 transactions per second. International Journal of Network Management, 30(5), e2099.

[26] Leng, Z., Tan, Z., & Wang, K. (2021). Application of hyperledger in the hospital information systems: A survey. IEEE Access, 9, 128965-128987.

[27] Dalla Palma, S., Pareschi, R., & Zappone, F. (2021, May). What is your distributed (hyper) ledger?. In 2021 IEEE/ACM 4th International Workshop on Emerging Trends in Software Engineering for Blockchain (WETSEB) (pp. 27-33). IEEE.

[28] Fan, C., Lin, C., Khazaei, H., & Musilek, P. (2022, August). Performance Analysis of Hyperledger Besu in Private Blockchain. In 2022 IEEE International Conference on Decentralized Applications and Infrastructures (DAPPS) (pp. 64-73). IEEE.

[29] Abdella, J., Tari, Z., Anwar, A., Mahmood, A., & Han, F. (2021). An architecture and performance evaluation of blockchain-based peer-to-peer energy trading. IEEE Transactions on Smart Grid, 12(4), 3364-3378.

[30] Tahmasbzadeh, A., & Kabirirad, S. (2023, May). A Blockchain-Based Approach for Data Storage in Drug Supply Chain. In 2023 9th International Conference on Web Research (ICWR) (pp. 335-341). IEEE.

[31] Pradhan, N. R., Singh, A. P., Kumar, N., Hassan, M. M., & Roy, D. S. (2021). A flexible permission ascription (FPA)-based blockchain framework for peer-to-peer energy trading with performance evaluation. IEEE Transactions on Industrial Informatics, 18(4), 2465-2475.

[32] Alam, M. J. C. T. (2016). Why the auto industry should embrace Blockchain. Car Tech.

[33] Jochumsen, M. L., & Chaudhuri, A. (2018, June). Blockchain's impact on supply chain of a pharmaceutical company. In EUROMA Conference (Vol. 6).

[34] Shih, C. W., & Wang, C. H. (2016). Integrating wireless sensor networks with statistical quality control to develop a cold chain system in food industries. Computer Standards & Interfaces, 45, 62-78.

[35] Tsang, Y. P., Choy, K. L., Wu, C. H., Ho, G. T., Lam, C. H., & Koo, P. S. (2018). An Internet of Things (IoT)-based risk monitoring system for managing cold supply chain risks. Industrial Management & Data Systems, 118(7), 1432-1462.

[36] Madhwal, Y., & Panfilov, P. B. (2017). Blockchain and supply chain management: Aircrafts' parts' business case. Annals of DAAAM & Proceedings, 28, 1051-1056.

[37] Kshetri, N. (2018). 1 Blockchain's roles in meeting key supply chain management objectives. International Journal of information management, 39, 80-89.

[38] Hulea, M., Rosu, O., Miron, R., & Aştilean, A. (2018, May). Pharmaceutical cold chain management: Platform based on a distributed ledger. In 2018 IEEE International conference on automation, quality and testing, robotics (AQTR) (pp. 1-6). IEEE.

[39] Singh, R., Dwivedi, A. D., & Srivastava, G. (2020). Internet of things based blockchain for temperature monitoring and counterfeit pharmaceutical prevention. Sensors, 20(14), 3951.

[40] Zhang, P., Liu, X., Li, W., & Yu, X. (2021). Pharmaceutical cold chain management based on blockchain and deep learning. Journal of Internet Technology, 22(7), 1531-1542.

[41] Gordon, W. J., & Catalini, C. (2018). Blockchain technology for healthcare: facilitating the transition to patient-driven interoperability. Computational and structural biotechnology journal, 16, 224-230.