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Blockchain-based smart tracking and tracing platform for drug supply chain

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ABSTRACT

The arising awareness of drug safety has brought tremendous demands on improving traceability and transparency in the supply chain. Conventionally, centralized/distributed database-based traceability platforms are adopted by many drug companies to control drug quality and improve transparency levels. However, it is still challenging to link drug stakeholders into an information-sharing chain due to the potential data manipulations and interest conflicts. In this context, this paper proposes a unified five-layer Blockchain and Internet of Things-based smart tracking and tracing (BIoT^3, in short) platform to provide a decentralized traceability solution in the drug supply chain. Following the five-layer blockchain platform architecture, a practical roadmap is provided for the drug industry to achieve blockchain design, development, application, and evaluation. Moreover, three core enabling components are presented: IoT-based drug identity management, on-chain & off-chain mechanism, smart contract-enabled drug services. According to the real data from collaborating companies, the feasibility and efficiency of the BIoT^3 platform have been verified using Hyperledger Fabric blockchain. The case study demonstrates that it not only gains useful insights into transaction sizes configuration for optimal blockchain performance, but also provides a feasible blockchain-based solution for drug traceability and visibility.

1. Introduction

Drug safety is always one of the biggest concerns since it directly influences public health. Researchers and industrialists widely acknowledge that an essential strategy to guarantee drug safety is to build a reliable drug traceability system ranging from drug production, logistics to sales (Klein & Stolk, 2018; Woodcock, 2016). According to *The British Standard*, traceability refers to the ability to track and trace the history, application, or location of an object (Alonso-Roris et al., 2016). The benefits of the drug traceability systems are increasing the protection of patients from falsified medicines and reducing the operational cost and time (Wimmers, 2015).

Previous studies on traceability systems mainly focus on two architectural modes: centralized mode and distributed mode. In centralized traceability mode, all the product-related data stored in a single database using web-based and IoT technologies to meet government regulation and consumer demands (Oztekin et al., 2010; Urbano et al., 2020). However, this centralized mode has been long questioned for its data security and scalability, especially when involving many parties with conflicting interests (Jing et al., 2014). To overcome these drawbacks, many researchers have developed distributed traceability mode. The distributed traceability mode refers to that each stakeholder (e.g., manufacturer, logistics provider, etc.) uses their database to store traceability information. A unified standard is adopted to provide data interfaces for data sharing in the distributed traceability mode (Lomotey et al., 2017; Munoz-Gea et al., 2010). However, the distributed traceability mode increases the maintenance cost and causes difficulties for reconfigurations, especially when involving system upgrades or updates, which is not suitable for small and medium enterprises.

Both approaches have some merits to achieve traceability in the drug supply chain. However, there are still some challenges when considering the intrinsic features in the drug supply chain. We summarize three main challenges as follows:

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- **Coexistence of transparency and privacy**. According to the investigation of the World Health Organization (2019), the public has the requirements for data transparency and visibility level in the drug supply chain. However, the drug manufacturers and distributors also have to protect their data security and privacy due to trade secrets, organizational policies, and many other considerations. As a result, consumers and regulators can only access limited drug information.
- **Concern between high safety requirements and inadequate product provenance.** The drug industry has one of the highest safety and regulation requirements (Casino et al., 2020). The practitioners must strictly comply with the stringent rules and standards, such as Good Manufacturing Practice (GMP), Good Supply Practice (GSP), etc. However, the reality is that there is inadequate trackable information. Take Changsheng Bio-tech as an example (Phillips, 2018), the vaccine maker has arbitrarily tampered the vaccine manufacturing operations rather than following GMP standards. All these disqualified vaccines circulate to the market, resulting in tremendous risks to consumers' health.
- **Dilemma between information dispersion and service integration**. Drug information is dispersed geographically in the supply chain (Luo et al., 2017). These dispersed drug data are hard to integrate to generate a consistent recording (Lopes-Martínez et al., 2018). Consequently, it leads to potential risks, such as counterfeit drug production, fake package recordings, and changing labels for polluted drugs in its circulation (Tseng et al., 2018). Therefore, it is necessary to build a decentralized service platform to integrate the disperse information.

To address the challenges, this paper proposes and develops a blockchain-based smart tracking and tracing platform to provide a decentralized traceability solution in the drug supply chain. Smart tracking and tracing, which are the operations revealing the drug trails from production to usage and vice versa, visualize the physical flow and information flow in the drug supply chain (Li et al., 2017). This requires the adoption of Internet of Things (IoT) technologies such as RFID, sensors, wireless communication technologies, etc., which helps build a smart environment to monitor the drug products being manufactured and distributed (Abdel-Basset et al., 2018). Furthermore, a reliable drug trail is required to introduce security and uphold drug recordings' immutability, which can be implemented using blockchain technology. Therefore, the objectives of this research include:

1) To propose a blockchain-based smart tracking and tracing platform that uses the abilities of blockchain and IoT technologies to support smart drug traceability.
2) To utilize the IoT solution combining QR code and RFID to achieve fine-grained identity management for drug items.
3) To design the blockchain-based data on-chain and off-chain mechanism for improving drug transparency level while keeping reasonable privacy.
4) To develop smart contracts for enabling a series of services, including quality regulation service, traceability and visibility service, and risk analytics & smart alert service.

The rest of the paper is organized as follows: Section 2 provides the relevant literature review. The architecture of BIoT^3 platform is proposed, as well as its key components in Section 3. Section 4 presents blockchain-based research & development (R&D) considerations for the drug supply chain. In Section 5, the case study is presented to illustrate the feasibility and efficiency of the proposed platform. Finally, the conclusion and further research are summarized in Section 6.

2. Literature review

Three streams of literature are reviewed to clarify the research gaps, including IoT-based traceability in drug supply chain, blockchain-based application in industries, and blockchain in drug supply chain.

2.1. IoT-based traceability in drug supply chain

Traceability refers to the ability to identify the origin and the various stages of goods and distribution processes (Alonso-Rorís et al., 2016; Sunny et al., 2020; van Donk et al., 2010). It tracks the product as its path through the supply chain and traces it back to its origin. Both Lovis (2008) and Attaran (2012) believe the traceability system could create values such as avoiding mistakes and fraud, protecting public health, and enhancing process management.

Researchers have conducted many studies to build IoT-based systems to achieve drug traceability and quality regulation. Initially, many studies explore the obstacles of drug traceability using RFID, such as technical communication interfaces, existing manual operations, and delayed supervision (Acierno et al., 2011; Evdokimov et al., 2011). Later, Zhao et al. (2014) studied an information-based real-time products management system based on IoT technologies. It efficiently collected the product flow information, providing valuable information for the materials and manufacturing enterprises. Similarly, Kong et al. (2019) proposed a veterinary drug quality and safety traceability system based on the cloud platform. It integrated the cloud service resources such as infrastructure, data service, and platform service to process data observation, vaccine product monitoring, and relevant information management.

However, the biggest problem of current drug regulation is the utilization of a centralized system that can hardly provide an open, trustable, and tractable environment. There is no adequate measure for consumers to fight back when faced with fraud, corruption, and data tampering (Wu et al., 2017). Recently, blockchain shows the potentials to solve these issues. Unlike the traditional centralized database management system, blockchain provides decentralized data storage, keeping data authentic and protecting data from tampering (Li et al., 2018; Vatankhah Barenji et al., 2020).

2.2. Blockchain-based application in industries

The concept of blockchain is proposed by Nakamoto (2009). Initially, it is a fundamental technology for digital currencies (e.g., bitcoin, Ethereum). Beyond its finance application, blockchain-based application in other industries is widely explored. This section reviews the blockchain-based traceability in the food, healthcare, and logistics industries since they share many similarities with the drug industry, such as quality assurance, safety-sensitive, multi-stage circulation, etc. (Casino et al., 2020).

2.2.1. Blockchain-based application in food industry

Food traceability has been an emerging blockchain application for improving anti-counterfeiting and quality assurance (Tsang et al., 2019). The implementation of blockchain can revolutionize the food industry by integrating traceability, authenticity, visibility, transparency (Creydt & Fischer, 2019; Rejeb et al., 2020). Both industrialists and researchers have explored the blockchain application in the food industry.

For example, IBM has been a pioneer in developing various applications of blockchain technology (Smith & Christidis, 2016). As the retail giant, Walmart used blockchain technology to track and trace the pork sourced from China (Higgins, 2017). In academia, many studies focus on using blockchain to increase food transparency and traceability for consumers. For example, Bumblauskas et al. (2020) designed the blockchain solution to track products from farm to fork using blockchain and internet of things (IoT) enabled technologies. Focusing on restaurant food traceability, George et al. (2019) proposed a restaurant prototype using blockchain and product identifiers. To identify boundary conditions for sharing assurance information to improve traceability, Behnke and Janssen (2020) have investigated four cases in the food supply chain using a template analysis of 16 interviews. The variety of boundary conditions suggests that organizational changes are needed before blockchain can be used successfully in the supply chain.

2.2.2. Blockchain-based application in healthcare industry

Healthcare industry is also embracing blockchain technology (Farouk et al., 2020). Blockchain has benefited the healthcare industry regarding accountability, traceability, and transparency (Clauson et al., 2018). Researchers identified that blockchain application covers three main areas: data management and exchange, contracts, and supply chain management (Gaynor et al., 2020).

For example, in medical data management, Chanchaichujit et al. (2019) introduced blockchain as an effective system to manage patient records and track medical drugs. Similarly, De Aguiar et al. (2020) discussed medical information management and sharing. The results show that many studies focus on sharing healthcare information using the practical Byzantine Fault Tolerance (pBFT) consensus algorithm and the Hyperledger Fabric platform. Kassab et al. (2019) provided a systematic literature review and found that blockchain could be implemented as a platform to improve the authenticity and transparency of healthcare data. As for the contract constructs, Khatoon (2020) has presented how a smart contract-based healthcare management system can be applied in the medical ecosystem for large-scale data management to streamline complex medical procedures.

2.2.3. Blockchain-based application in logistics industry

Blockchain is regarded as a significant impetus in the logistics industry (Hackius & Moritz, 2017; Verhoeven et al., 2018). Blockchain can be used to build a traceable and identifiable system for the logistics industry from production, warehousing to distribution (Helo & Hao, 2019). To understand the various blockchain application in logistics, exiting research has been classified into three clusters: information security, product transport, and logistics management (Dobrovnik et al., 2018; Issaoui et al., 2019; Pournader et al., 2019).

For instance, Fu and Zhu (2019) used blockchain technology to build an intelligent logistics system to solve information security threats. It provided thought for applying intelligent logistics systems based on blockchain. As for product transport, to provide consistent and satisfactory services for customers in modern logistics, blockchain has been applied to container shipping to track the tens of millions of transactions involving shipping containers globally spanning the entire supply chain (Groenfeldt, 2017; Hasan et al., 2019). More recently, Sunny et al. (2020) presented a practical blockchain-based traceability solution using Microsoft Azure Blockchain Workbench for a cold chain scenario. Finally, in logistics and supply chain management, Li et al. (2019) explored blockchain's potential application in logistics to facilitate supply chain management for both suppliers and consumers. Similarly, Ar et al. (2020) proposed a decision framework based on a multi-criteria decision structure incorporating AHP into VIKOR under Intuitionistic Fuzzy Theory to explore feasible blockchain-based operations in the logistics industry. The findings suggest that the most viable logistics operations proved to be transportation, materials handling, warehousing, order processing, and fleet management in possible blockchain implementation. Moreover, Orji et al. (2020) proposed a technology-organization-environment theoretical framework of critical factors that influence the successful adoption of blockchain technologies in the freight logistics industry.

2.3. Blockchain in drug supply chain

Researchers have conducted many insightful investigations and explorations to step forward blockchain application in the drug supply chain. They could be streamlined into three categories: identification of blockchain success factors and benefits, design of conceptual architecture and mechanism, and initial implementation of the blockchain-based solution.

In the early explorations, researchers have identified the possibility, success factors, and benefits of applying blockchain in the drug industry. For example, Mottaeva et al. (2018) explored the prospects for blockchain in the pharmaceutical market. Later, Sinclair et al. (2019) examined how blockchain can be applied to meet the security compliance requirement for the pharmaceutical supply chain. To identify the success factors of applying blockchain in the pharmaceutical industry, Fernando et al. (2019) provided a review using the *meta*-analysis method. The result found that five dominant factors in the application of blockchain technology are Track, Trust, Traceability, Transparency, and Real-Time. With the clarity of blockchain's benefits and potentials, many researchers have designed the blockchain-based conceptual architecture and mechanism to control counterfeit and poor-quality drug products in the drug supply chain. For example, blockchain has been used to add traceability, visibility, and security in the drug supply chain to prevent counterfeit drugs (Muselemu & Haq, 2018). Focusing on the drug distribution stage, Sylim et al. (2018) developed a pharmacy surveillance blockchain system and tested its functions in a simulated network. To control the illegal sales of medication in Latin-America, Molina et al. (2019) proposed Blockchain technology to solve traceability problems and lack of control in the drug trade. Some of the researchers also achieved some initial implementation of blockchain-based systems in the drug industry. Jamil et al. (2019) developed a novel drug supply chain management using Hyperledger Fabric blockchain to handle secure drug supply chain records. Similarly, Abbas et al. (2020) proposed and implemented a novel blockchain and machine learning-based drug supply chain management and recommendation system. Benita et al. (2020) used the smart contract running on a public Ethereum network to tracking drug circulation. An IoT sensor-based blockchain framework is proposed that tracks and traces drugs as they pass slowly through the entire supply chain, focusing on securities and scalability analysis (Singh et al., 2020). After analyzing the impact of counterfeit drugs, Saxena et al. (2020) build an Ethereum blockchain-driven tool using Amazon Web Service, named PharmaCrypt.

In summary, the traceability of the drug supply chain is vital but complex. The centralized traceability systems have exposed many issues such as data tampering, information opaqueness, etc. Blockchain shows the potentials to overcome these issues with distinctive features such as immutability, transparency, security, etc. (Liu et al., 2020). However, blockchain in the drug supply chain is still in its infancy (Sunny et al., 2020). Most researches are related to initial blockchain explorations, design, and implementation, such as the potential benefits, workflow design, experimental simulation. More efforts are still needed to provide a systematic roadmap on developing, implementing, and applying blockchain to achieve traceability and transparency in the drug supply chain. Moreover, there is a lack of blockchain-based implementation using real data from drug circulation. Therefore, we present a blockchain-based smart tracking and tracing platform combining blockchain and IoT technologies to achieve an open, secured, and integrated drug supply chain.

3. Overview of proposed BIoT^3 platform

This section discusses the architecture of the BIoT^3 platform and its key components, including IoT-based identity management, blockchain gateway, and smart contract and its mechanism.

3.1. Architecture of proposed BIoT^3 platform

Fig. 1 presents the architecture of the BIoT^3 platform. It consists of five layers: the perception layer, off-chain layer, blockchain layer, application layer, and user layer.

The perception layer is used to collect multiple data in the drug supply chain. It consists of various smart IoT assets, e.g., QR code, RFID tags, and readers, sensors, etc. Notably, the typical scenario of the drug

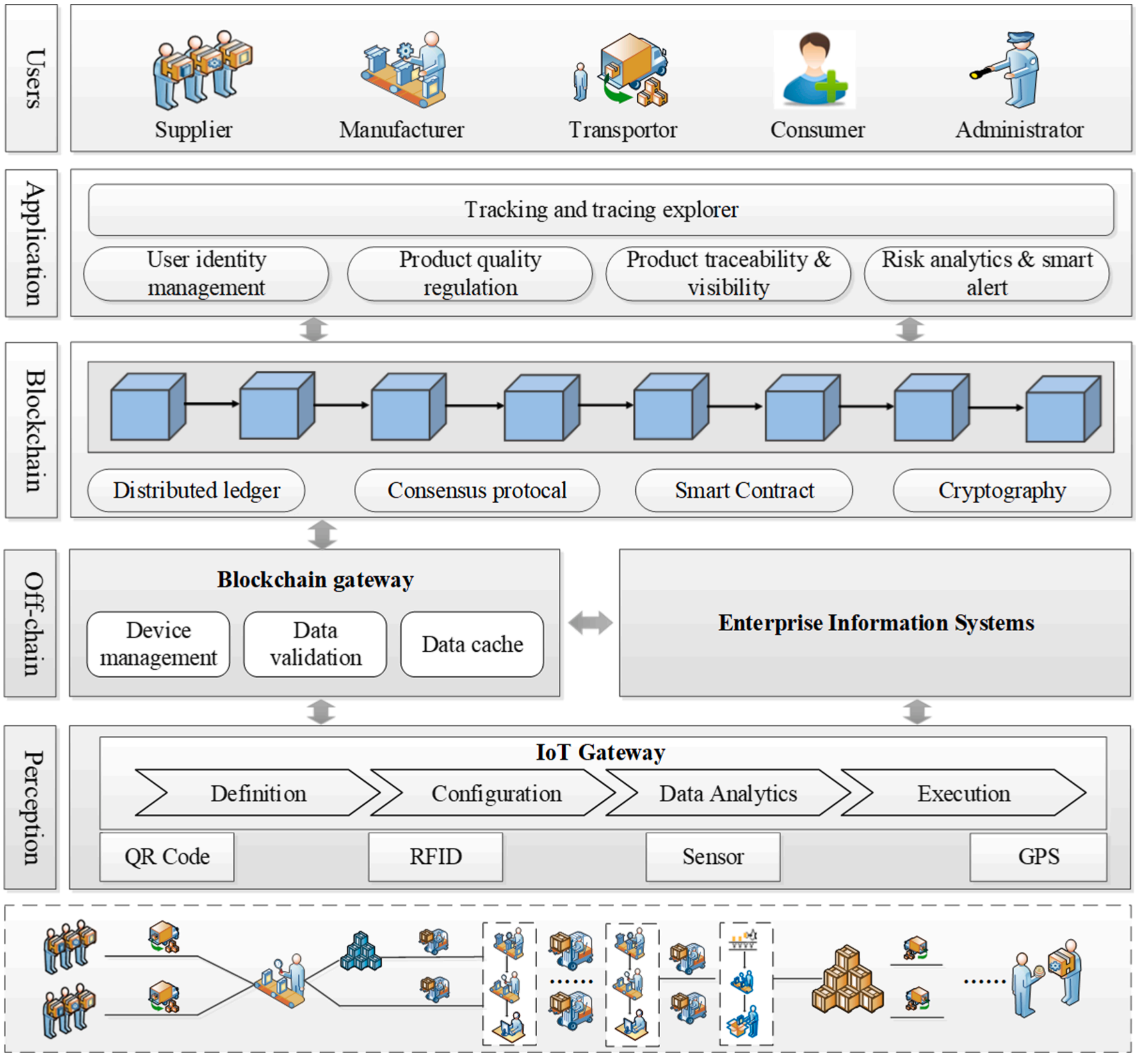

Fig. 1. The architecture of BIoT^3 platform in drug supply chain.

supply chain is shown at the bottom of Fig. 1. The collected data will be transferred to the IoT gateway. Notably, IoT gateway defines, configures, and analyzes the data, such as the origin of raw material, drug manufacturing data, drug logistics data, etc. Those data have three typical features: constant accumulation, the large data scale, and continuous refinement of data granularity.

The core of the off-chain layer is the blockchain gateway, which serves as a middleware. It has three critical components, including device management, data validation, and data cache. Device management refers to each IoT device having a unique identity, such as public and private keys. The managers of the blockchain gateway are responsible for adding, deleting, and updating device states. The data validation is conducted to verify the transaction data structure and device identity. Data storage is used to store transaction data until the data uploaded to the blockchain network. The input data of the blockchain gateway comes from two parts: IoT assets and enterprise information systems. The format of the input data is predefined using a JavaScript Object Notation (JSON) file. The outputs of the blockchain gateway are the transactions to the blockchain network from drug stakeholders.

The blockchain layer contains consensus, smart contract, cryptography and peer-to-peer (P2P) network, etc. In this research, we choose pBFT as the consensus. It can provide a highly efficient and effective consensus method in the regulation process (Vatankhah Barenji et al., 2020). Smart contracts are stored, replicated and supervised by the network of nodes that run the blockchain. The smart contract plays a role in assessing the quality information in the blockchain platform. Cryptography is used to guarantee the security of information broadcasting. The P2P network is a distributed network structure that fits the multiple nodes in the drug supply chain.

The application layer consists of four services: user identity management service, quality regulation service, product traceability & visibility service, and risk analytics & smart alert service. The tracking and tracing explorer provides the interfaces for different users to inquire the relevant drug data, which interact with the blockchain network through application programming interfaces (APIs). For example, quality regulation service means that the drug producers need to provide their legal certifications (e.g., Good Manufacturing Practice (GMP), Good Supplying Practice (GSP)). For product information traceability, the consumer can search drug circulation history through the tracking and tracing explorer. Risk analytics & smart alert service is used to achieve smart analysis and warnings. The user identity management is used by senior manager of this blockchain system to manage the members, such as adding, deleting, and updating.

The user layer consists of four user groups, including drug producers, drug logistics providers, pharmacists, and consumers. In the drug production phase, producers need to attach electronic codes to the produced drugs and upload their quality-related data to the blockchain. In the drug distribution stage, the logistics providers need to detect various drug storage parameters, such as temperature and humidity, and store these parameters in blockchain, ultimately achieving a complete chain of drug supply chain information. Simultaneously, the quality regulators can quickly obtain the drug quality information through the blockchain-based platform. Users can use this platform to search drug quality information and receive timely feedback on adverse events.

3.2. Key components of BIoT^3 platform

To better understand the proposed platform's mechanism, we present the three key components, including IoT-based identity management, blockchain gateway, and smart contracts mechanism.

3.2.1. IoT-based identity management

Fig. 2 presents the IoT-based identity management system to provide a fine-grained drug item traceability. It consists of four sub-levels: item-level, box-level, pallet-level, and truck-level. For the item-level, the drug item is the fundamental element on which QR code is printed. The QR code is like an identity card to a specific drug item, which contains basic drug origin information such as the identity number, raw materials, quality information, production conditions, etc. As for the rest three levels, RFID tags are used to attached to different levels of boxes to facilitate traceability in logistics and distribution. Hand-held reader and fixed RFID reader are used to collect the drug logistic data. For example, the hand-held reader collects the assembling information, circulation information, transaction information, and disassembling information. The data collection processes are presented below.

Firstly, the sensors, RFID devices are used to collect the data in drug manufacturing and logistics. The collected data are sent to the IoT gateway (Fang et al., 2013). The connectivity protocols between those sensors and smart gateway are usually wireless-based protocols, such as Wi-Fi, Bluetooth, etc. Secondly, the IoT gateway can play a role in storing and pre-processing the raw data. Thirdly, the pre-processed data transfers to the off-chain layer, including blockchain gateway and enterprise information systems. The messaging protocols are Plain HTTP, MQTT, etc. The data flow in the blockchain gateway is described in the following section.

3.2.2. Blockchain gateway

Blockchain gateway is a light-node in Hyperledger blockchain and plays the role as middleware for data on-chain/off-chain storage. For the perception layer, the blockchain gateway manages the IoT devices, such as the sensor device, smart readers, and IoT gateway. The device management module provides each IoT device with a unique identity, including public and private keys. The managers, who are responsible for IoT devices, can manage these devices by publishing the authorization list of devices through blockchain gateway, so that manager can use the blockchain gateway to add, delete and update device states in the blockchain network. The manager can then add/delete IoT devices by launching a transaction that records the public keys of the authorized IoT devices.

For the blockchain layer, the blockchain gateway determines the connection parameters, such as channel, orderer, and organization through the defined SDK. Fig. 3 illustrates the mechanism of data on-chain and off-chain storage using blockchain gateway. Based on the on-chain/off-chain mechanism, the private data needs to store in the cloud/IPFS, and its hash value stores in blockchain, such as drug manufacturing process information. The data with less privacy needs to put directly in on-chain, such as the raw material origin, GMP, GSP, etc. Notably, only the transaction data between different stakeholders can change the world state. The general data which describes the physical drug supply chain, such as temperature and humidity, will be only stored in ledgers.

3.2.3. Smart contract and its mechanism

Fig. 4 illustrated four types of smart contract-enabled applications, including pharmaceutical manufacturer and logistic service provider (Application 1), intra-logistics service providers (Application 2), logistic service provider and pharmacy (Application 3), and pharmacy and customer (Application 4). Three algorithms are designed for the smart contract-enabled applications to facilitate drug circulation among different stakeholders, as shown below.

Algorithm 1 describes smart contract process of application 1, which is related to drug enterprises and logistic services. The drug enterprise starts the process with triggers an event that leads to a change in the Drug contract state "product sent". This allows the first phase of the contract to take place. If anyone else tries to launch or begin the contract except drug enterprise manager, the error will happen in the contract then the state of the contract will change to original state.

Algorithm 1. Smart contract between manufacturer and logistics provider

Smart contract 1: Manufacturer and logistics provider
Input: Seller, Buyer, DrugState, Manufacturer, LS1
Output: The updated contract state between manufacturer and logistic provider
if (seller == Manufacturer) **then**
  if (DrugState != create) **then**
    Let DrugState = OrderToBeCreated.Manufacturer;

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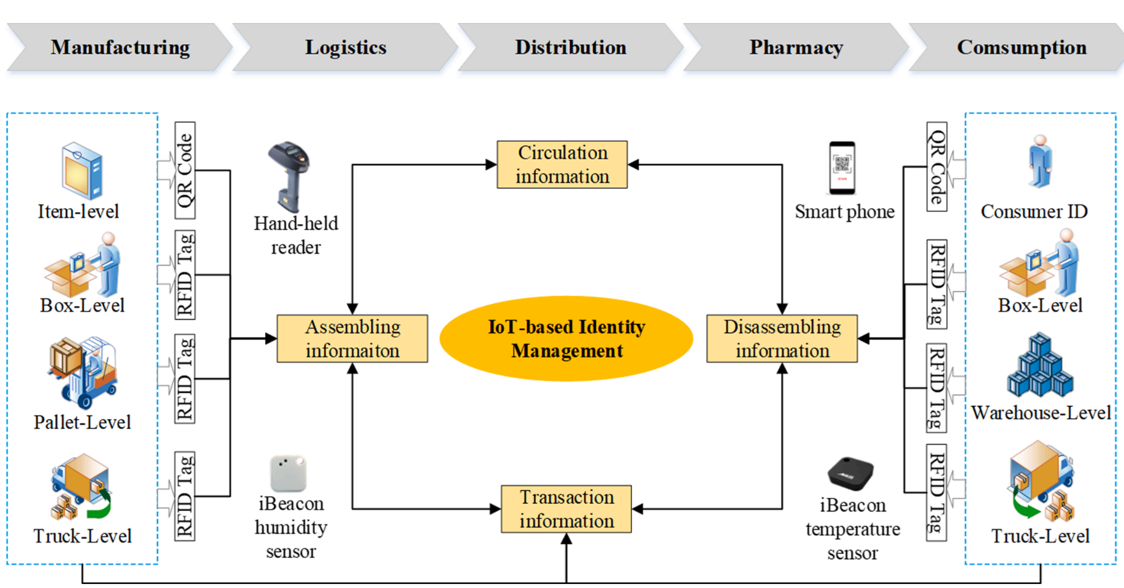

Fig. 2. IoT-based unique identity management.

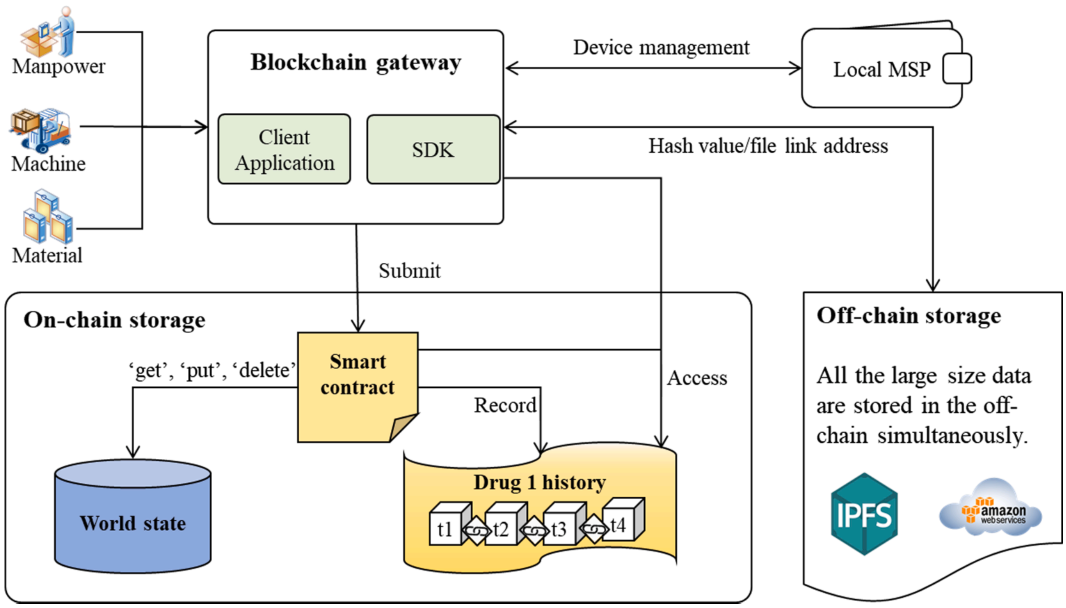

Fig. 3. The mechanism of data on-chain and off-chain storage.

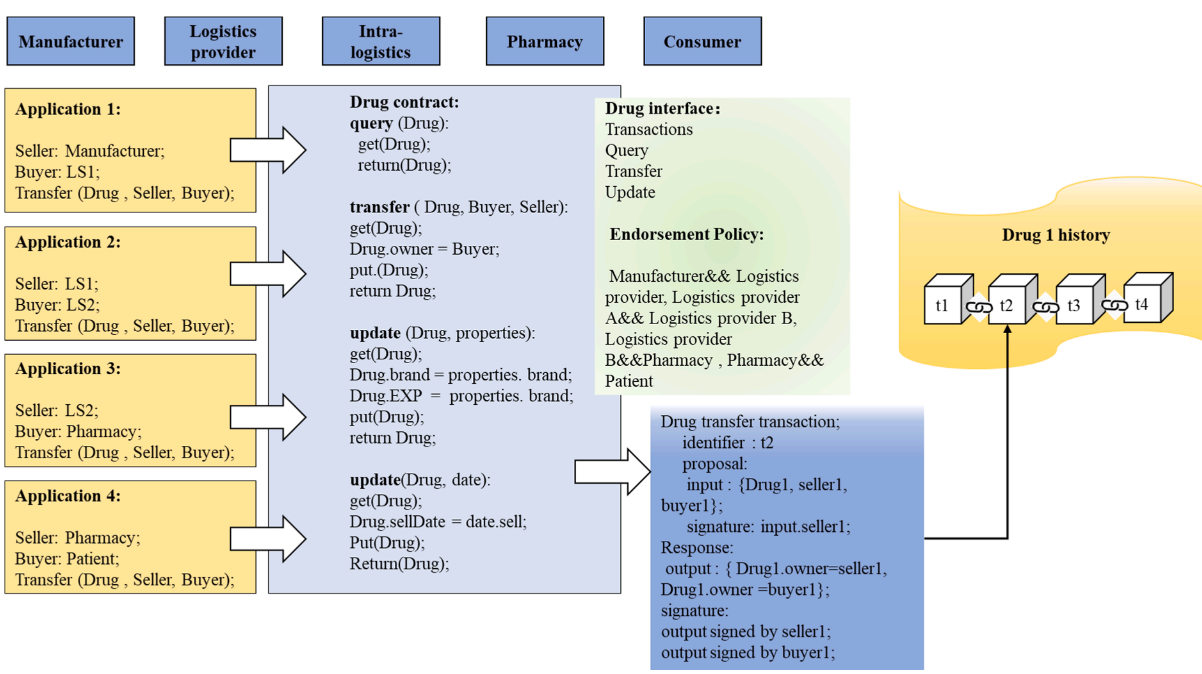

Fig. 4. Proposed smart contracts based on Hyperledger Fabric.

(*continued*)

Algorithm 1. Smart contract between manufacturer and logistics provider

```
      Manufacturer initiates to create process;
      Request sends to LS1;
    else if (DrugState ==create and buyer == LS1) then
      DrugState update and order received by LS1;
    else if
      Show an error and update contract state;
    else
      Show an error and update contract state;
  end
```

Algorithm 2 explains the smart contract of application 2, which is related to logistic service providers. It is initiated by updating the state of the DrugState to intra-logistic phase. This smart contract is responsible for creating and sending the notification to all participating in the platform. The smart contract makes the sellers know that the drug is sent to a specific logistic service provider.

Algorithm 2. Smart contract for intra-logistics providers

Smart contract 2: Drug state for intra-logistics providers
Input: Seller, DrugState, LS, Intra-LS, outcome
Output: The updated contract state of newest drug logistics state

```
if (seller == LS1) then
  if (DrugState != UpdatebyLS) then

    if (outcome== True) then
      Let DrugState = Intra-LS;
```

(continued on next page)

(*continued*)

Algorithm 2. Smart contract for intra-logistics providers
Create and send a notification about the start of the logistic service;
else if
Next step cannot start, update status to the system;
else if
Show an error and update contract state;
else
Show an error and update contract state;
end

Algorithm 3 explains smart contract of application 3 between logistics service provider and pharmacy. Once the logistic service is completed, the logistics service provider checks the details and signs with approval and next step is started. If the logistics service provider is not able to support the chain on the system for any reasons or issues, the state of the DrugState is not updated.

Algorithm 3. Smart contract for intra-logistics providers
Smart contract 3: Drug state for logistics providers and pharmacy
Input: Seller, DrugState, LS, Intra-LS, Pharmacy, Outcome
Output: The updated contract state in pharmacy stage
if (seller == LS) **then**
if (DrugState != UpdatebyPharmacy) **then**
if (outcome== True) **then**
Let DrugState = Pharmacy;
Create and send a notification about the end of the logistic service;
and arriving to specific pharmacy;
else if
Next step cannot start, update status to the system;
else if
Show an error and update contract state;
else
Show an error and update contract state;
end

The last smart contract is between pharmacy and customer, which is a simple smart contract updated by the pharmacy based on the prescription. In this step, the prescription acts as a reference and update to the platform.

4. Blockchain-based R&D considerations

This section presents the considerations of blockchain-based R&D for the drug supply chain, including existing blockchain platform considerations, data representation and storage, external systems integration.

4.1. Existing blockchain platform considerations

To explore suitable blockchain in the drug supply chain, we compare two typical blockchain platforms: Ethereum and Hyperledger Fabric, as shown in Table 1. Ethereum is a decentralized platform that runs smart contracts precisely as programmed without any possibility of downtime or third-party interference (Wood, 2014). Hyperledger is an open-sourced community to benefit an ecosystem of Hyperledger-based solution providers and users, focusing on the use cases across various industrial sectors (Cachin, 2016). The following parameters are considered: network type, cryptocurrency, consensus mechanism, and smart contracts, since they are the core components of blockchain application.

Table 1
Comparison of Ethereum and Hyperledger Fabric blockchain.

Comparison	Ethereum-based blockchain	Hyperledger Fabric blockchain
Network type	• Public • Consortium • Private	• Consortium
Cryptocurrency	• Ether; • Token via smart contract	• Tokens via chaincode
Consensus mechanism	• PoW • Ledger level	• pBFT/Raft • Transaction level
Smart contracts	• Smart contract code (e.g., Solidity)	• Chaincode (e.g., Go, Java)

According to the comparison, it is found that Ethereum-based blockchain has more flexible network types and cryptocurrency selections, while Hyperledger-based blockchain is mainly focusing on the consortium blockchain and tokens are issued via chaincode. On the other hand, Ethereum's consensus is mainly based non-trust-based algorithms, such as Proof of Work, Proof of Stake, and all the members can access the block data in the same ledger. At the same time, Hyperledger-based blockchain has a more flexible setting in consensus selection and ledgers' configuration.

Based on the findings, we choose the Hyperledger Fabric as the development platform for the drug supply chain for three reasons. First, Hyperledger Fabric provides a more flexible chain structure. To achieve flexible collaboration and privacy control in the drug supply chain, a different group of stakeholders can form their consortium in Hyperledger Fabric by sharing their ledger. Second, Hyperledger Fabric could adopt more trust-based consensus algorithms, such as pBFT, raft, etc. It could guarantee a high system performance considering the massive data volume in the drug supply chain. Third, a chaincode-based workflow application is also suitable enough for drug traceability management.

4.2. Data representation and storage

Drug industry involves many stakeholders, including manufacturers, distributors, sub-distributors, pharmacists, consumers, etc. Each stakeholder has a massive amount of data to integrate, interoperate and share, such as suppliers, raw material quality information, manufacturing processes, drug manufacturers information, GMP/GSP certificate. The data format could be represented as text, time and date, location, image, URLs, etc. Some of these data are highly sensitive and private, which could only be available to a specific range of stakeholders. Therefore, it is necessary to consider the principles "what kinds of data will be stored on-chain, while the other is off-chain."

Ideally, there are two possible solutions to achieve the on-chain and off-chain principles (Longo et al., 2019; Xu et al., 2019). One is to put raw data off-chain and the hash of the raw data on-chain. The other is to put encrypted data on-chain and the decrypted key off-chain. The first one has many advantages, like saving the block size, improving the system performance, keeping the data privacy. At the same time, it also introduces the uncertainty of a single point of failure. The second solution can provide reliable data storage and secured sharing, but it might affect the system performance and harm the data privacy if the cryptography is not safe anymore. Therefore, in this paper, we choose the first solution: storing raw data off-chain and storing metadata, small critical data, and hashes of the raw data on-chain. It guarantees the blockchain system performances in data storage and computation and meets the data privacy requirements of the drug stakeholders. Based on the proposed principles, we make a guidance for data on-chain or off-chain in drug scenarios, as shown in Table 2. Privacy and amount are chosen as the standards in the drug industry.

4.3. External systems integration

Drug processes and activities often need various enterprise information systems (EISs) to integrate data, optimize decision-making, and timely monitor and manage, such as MES, SCM, ERP, etc. Therefore, the development of blockchain must consider the integration with these existing systems in the drug industry.

It should be ensured that the blockchain network is capable of accessing data outside of its own network. These data can enrich the

Table 2
On-chain vs. Off-chain samples in drug blockchain.

Data type	Privacy	Amount	On-chain vs. Off-chain
Raw material quality data	Low	Middle	On-chain
Quality data	Low	Middle	On-chain
Drug manufacturing process information	High	Middle	Off-chain
Packaging data	Middle	Large	On-chain
Drug manufacturer information	Low	Small	On-chain
Pharmaceutical logistics provider	Low	Small	On-chain
Drug storage information (temperature, humidity, etc.)	Low	Large	Off-chain
GMP&GSP certificates	Low	Small	On-chain

values for blockchain-based drug traceability workflows. Similarly, it is also necessary to ensure that external systems can communicate with the blockchain network to facilitate collaboration and sharing among different drug stakeholders. One way to achieve this is to set up an external event hub, which acts as a medium to exchange data with external systems through event processors. The external application can listen to specific events from the hub and perform certain tasks accordingly. We leverage Axios APIs to build a unified connection with the existing systems, including enterprise information systems integration, IoT integration, etc.

5. Case study

To evaluate the feasibility and efficiency of the BIoT^3 platform, the case study is conducted as following three aspects: (1) collecting real data from our collaborating drug company; (2) developing the BIoT^3 platform along with the key services; and (3) applying and evaluating the developed platform and services using the real data.

5.1. Scenario description

Fig. 5 presents the drug circulation scenario based on the collaborating company with real data related to drug logistics time interval. The scenario contains three drug manufacturers, three logistics service providers, six pharmacies, and ten customers. These stakeholders are geographically distributed among three countries, including China, Singapore, Malaysia.

Three functional requirements are identified based on the initial investigation. The first requirement is product traceability and visibility. Both manufacturers and customers are often eager to trace a complete data history along the drug life cycle to increase transparency and facilitate drug safety. The second requirement is drug quality regulation. During the drug circulation process, manufacturers always make strategies to prevent the impact of expired drugs or drug fleeing to maximize the business value. The third requirement is risk analytics and smart alert. Since the increasing numbers of drug safety incidents, it is necessary to provide necessary safety analytics/alert service during the sales process. Drug companies need to collect real-time data/feedback to analyze the potential risks and make corresponding emergency measures.

To meet above requirements, the BIoT^3 platform is proposed and developed. Simulated experiments were conducted by considering two different scenarios: a) without counterfeit medicine transfusion, and b) with counterfeit medicine transfusion. We consider counterfeit drug transformation by the LS2 in the second scenario.

5.2. Development and implementation of BIoT^3 platform

To present the whole development process, this section explains prerequisites, development environments, and technologies used for the implementation of the BIoT^3 Platform. We chose Hyperledger Fabric as a development platform. It is a distributed ledger solution built upon a modular architecture with high degrees of confidentiality, resiliency, flexibility, and scalability. We configure the fabric environment by downloading the Fabric-sdk-java toolkit, and use IntelliJ IDEA as the development IDE. We also use the golang language as the main development language for smart contracts with ChainCode toolkit to write related smart contracts. The consortium and permissioned blockchain are developed based on the following parameters, which contains two virtual machine (VM) and each VM has two virtual CPU cores, 4 GB of memory and 10 GB of persistent storage and a physical machine with Intel Core i7, 16 GB of memory. Elastic search was used to store block-related information. The behavior of network monitored by the Python Web3 Library. We have set and updated our network in the form of transaction with following on-chain protocol. For configuration of network, various Docker containers for various network entities like peers, orderer, client, and MSP are used. All the configurations store Docker compose file. In addition, we built one container for each transaction in the scenario shown in Fig. 6. REST API for network is implemented by Node.js. Table 3 shows the attribution behind of the developed platform.

Client side of application is developed with Bootstrap. It is a free and

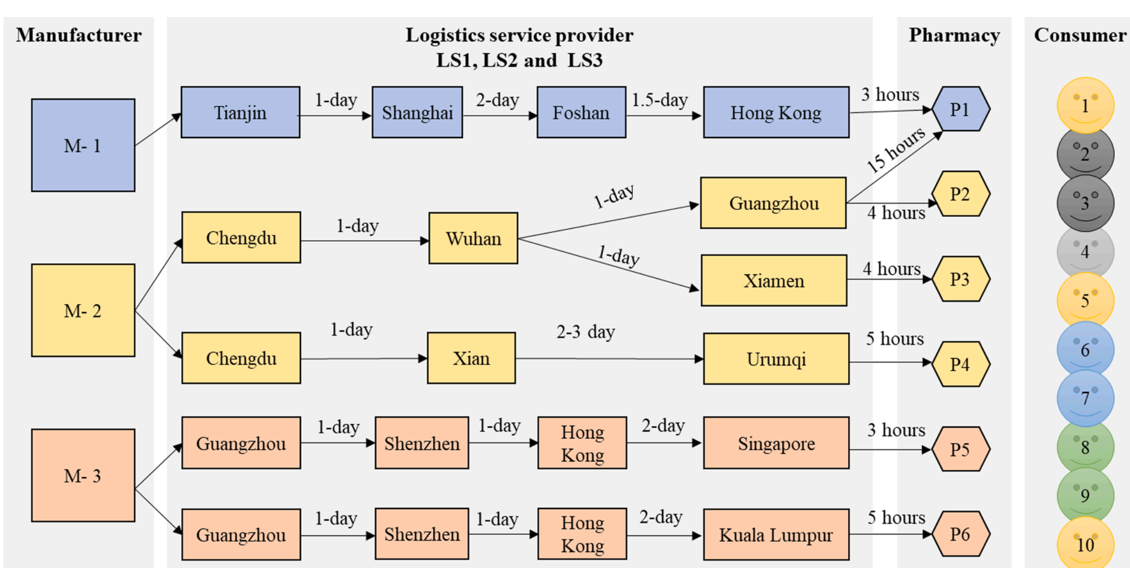

Fig. 5. Case scenario description in drug supply chain.

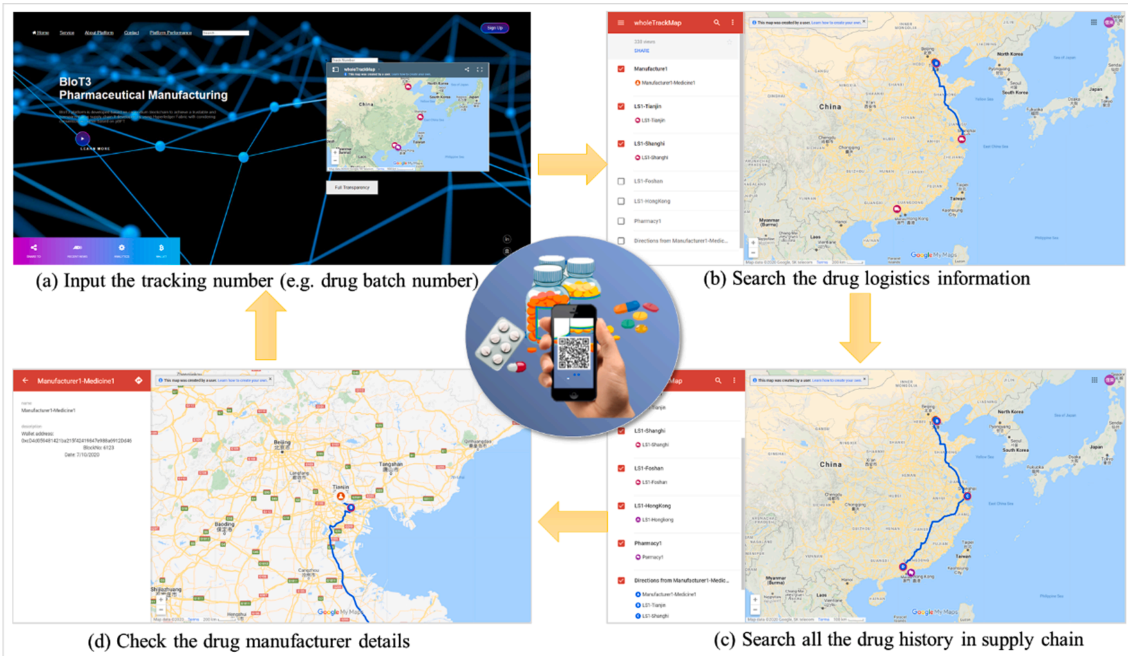

Fig. 6. The interfaces for drug traceability and visibility service.

Table 3
The development environment and attributions of the BIoT^3 platforms.

Component	Sub-component	Description
IDE	IntelliJ IDEA	IntelliJ IDEA is used as the integrated development environment
Blockchain Backend	Experimental environment	Two virtual machines (Ubuntu Linux 14.04, 2 CPUs, 4 GB RAM, 10 GB ROM)
	Storage of block information	Elasticsearch
	Network behavior monitor	Python Web3 Library
	Blockchain type	Hyperledger Fabric
	Consensus algorithm	pBFT
	Asymmetric Cryptography algorithm	ECC Encryption is used for the generation of private and public keys.
	Hash algorithm	SHA256 is used to generate the digital signature.
	Cryptographic hash function	RIPE Message Digest is used for hashing addresses.
	Networking protocol	Gossip protocols are used for creating the peer-to-peer network.
Application Frontend	Bootstrap (CSS, JavaScript)	Bootstrap is used as the tool to develop the frontend application

open-source CSS framework directed at responsive, mobile-first frontend web development. It contains CSS and JavaScript-based design templates for typography, forms, buttons, navigation, and other interface components.

5.3. Application of key services

This section focused on applying key services, including product traceability and visibility service, drug quality regulation, and risk analytics & smart alert service.

5.3.1. Product traceability and visibility service

Fig. 6 shows the interfaces of the product traceability and visibility service from a customer perspective. Firstly, the customer needs to scan the QR code or input the tracking number in the *tracking and tracing explorer,* as shown in Fig. 6 (a). Secondly, the customer could receive the drug logistics information with the map for detailed drug history information. By selecting *wholeTrackMap,* customers will get access to whole tracking information via Google Maps. Thirdly, the customer could select a relevant checkbox to check the detailed drug information at a specific phase, such as manufacturing, distribution, etc. Finally, by selecting the transaction, customers will get access to detailed information such as wallet address, block number, and quality control data, as the following figure shows the *Manufacturer1* and *LS1-Tianjin* transactions. Block number and wallet address for each transaction is accessible as the unique proof of drug circulation. *Manufacturer1* transaction shows that *Medicine1* is produced by this company with associate wallet address of "*0xcD4d05 9481421ba215f42419847e988a6912Dd46*" that is store in the BlockNo "*6123*" and connected related off-chain data. *LS1-Shanghai* transaction shows this medicine was arrived in Shanghai by *LS1-Tianji*. This transaction store in the BlockNo"*6125*" with wallet address associate to *LS1-Shanghai* "*0x8 eF8b7183d2892E9eC673cbacC1f4d 3dd3D97016*". This shows that BIoT^3 can track the inter-logistic transactions and brings transparency to the inter-logistic process. By this, it created more reliable information recording, which is provided by certification regulation service for consumers.

5.3.2. Product quality regulation service

Fig. 7 presents the illustration of drug quality regulation service along the life cycle. The contents in the bubbles of Fig. 7 include block address, date, and block number. The information shows the generated block information in our experiment, which uniquely identifies the drug item in the drug supply chain. Four key stakeholders include manufacturers, logistics service providers, pharmacists, and consumers. When the drug stakeholders receive a drug item, the drug information will be uploaded to the blockchain. The "block address" identifies whom the drug belongs to. The "block date" shows when the drug arrives. And the drug location is explicitly presented in Fig. 7. As a result, a whole drug life cycle is connected. It helps the manufacturer perceive the status and location of drugs and facilitates product quality regulation.

5.3.3. Risk analytics & smart alert service

Fig. 8 presents the risk analytics & smart alert service. Three fishbone timelines represent the drug traceability recordings from the initial point to the endpoint. Based on the visualized information, it is clear

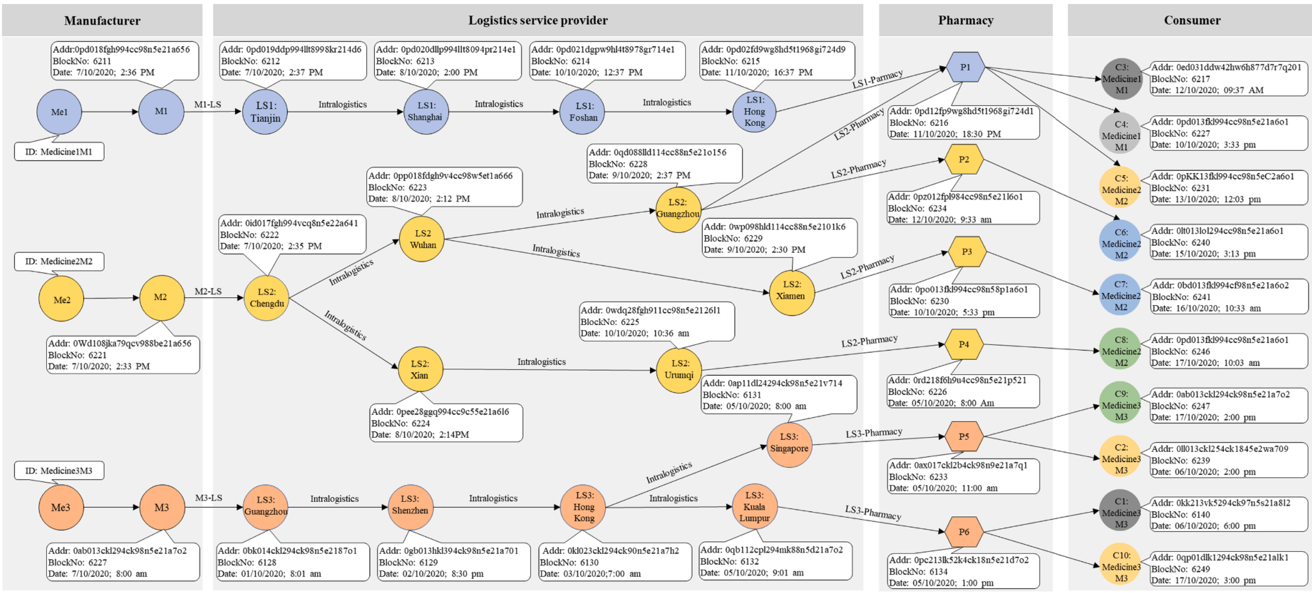

Fig. 7. Illustration of drug quality regulation along the life cycle.

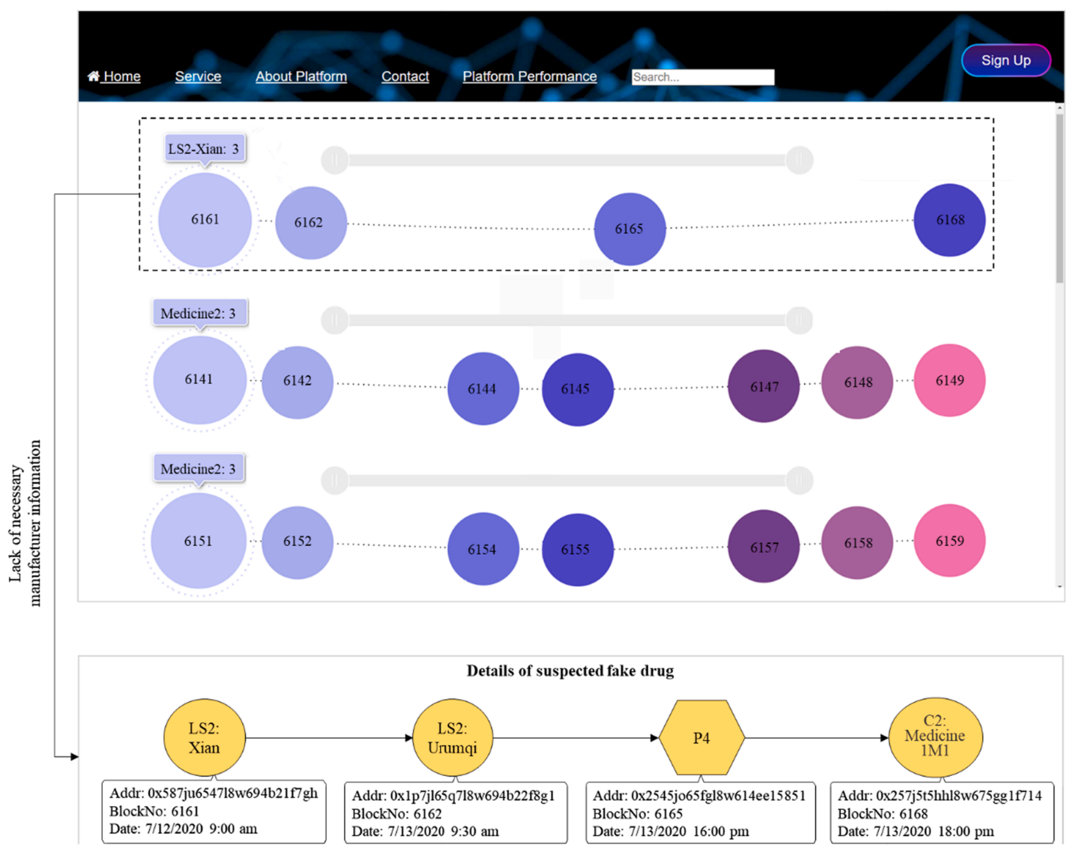

Fig. 8. Interfaces for risk analytics and smart alert service.

that the first graph is different from the others due to the lack of drug manufacturers. Using the risk analytics & smart alert service, the consumer could find that the counterfeit drug transfusion is probably happened at Xian city by LS2. For detail, this medicine was purchased by customer 4 from pharmacy 4. These transactions occur because logistics service providers act as MSP in the platform. Therefore, it is clear that this platform's openness delivered a very effective tracking system for all users. The alert information could be sent to customer 4.

5.4. *Evaluation of the proposed BIoT^3 platform*

The experimental evaluations are conducted based on qualitative and quantitative comparisons. The qualitative comparison analyzes typical criteria between the proposed BIoT^3 platform with the other traceability platforms. The quantitative analysis compares the proposed BIoT^3 platform (Vatankhah Barenji et al., 2019) with a specific blockchain-based ubiquitous manufacturing (BCUM) platform. Notably, the objectives of the evaluation are two-fold: 1) to illustrate the feasibility and efficiency of the proposed BIoT^3 platform; 2) to clarify the differences between the BIoT^3 platform with existing traceability solutions.

In the qualitative comparison, Table 4 presents the results of the typical criteria comparison between the proposed BIoT^3 platform with four existing traceability solutions. The existing traceability solutions include IoT-based centralized traceability platform, IoT-based distributed traceability platform, and cloud-based traceability platform, blockchain-based traceability platform. The comparison criteria are selected based on the existing literature of traceability systems, such as scalability, transparency, security, etc. The results are summarized below to clarify the differences between existing traceability solutions with the BIoT^3 platform.

In the quantitative comparison, we compare the proposed BIoT^3 platform with the BCUM platform (Vatankhah Barenji et al., 2019). We choose the BCUM platform because of two reasons. Firstly, both blockchain platforms share a similar blockchain configuration and infrastructure setup, such as blockchain type, running environment, etc., as shown in Table 3. Secondly, the BCUM platform represents a typical blockchain application by evaluating throughput and response time. Table 5 presents the compared elements between BIoT^3 and BCUM platforms, including application scenario, target user, smart contract, and performance analysis.

1) Application scenario

BIoT^3 platform aims to provide traceability solutions into the drug supply chain, while the BCUM platform aims to bring decentralized manufacturing for ubiquitous manufacturers distributed geographically.

2) Target user and smart contract

The target users of the BIoT^3 platform include the main stakeholders in the drug supply chain, such as the producers, logistics providers, intra-logistics providers, pharmacists, and consumers. Therefore, we designed four types of smart contracts to facilitate drug circulation, as presented in section 3.2.3. In contrast, the target users of the BCUM platform include manufacturers (e.g., service providers) and consumers (service demanders). A type of smart contract is designed to connect the service providers and end-users.

3) Performance analysis

The performance analysis of the BIoT^3 platform evaluates the impact of transaction size on transaction response times to explore the suitable block size (Kilobyte, kB in short) for the blockchain network. To our best knowledge, this paper is the first to explore the suitable block size for industrial applications. In contrast, the BCUM platform evaluates throughput and the impact of data size (transaction per second, tps in short) on response time to test the effectiveness. Therefore, there are distinct differences in performance analysis. The detailed performance analysis of this paper is presented below.

Table 5
The quantitative comparison between BIoT^3 and BCUM platforms.

	BIoT^3 platform	BCUM platform
Application scenario	Traceability solution for drug supply chain	Decentralized solution for ubiquitous manufacturing
Target user	Five types of stakeholders (e.g. manufacturer, logistics provider, intra-logistics provider, pharmacist, end consumer)	Two types of stakeholders (e.g. 3D printing service providers, service demanders)
Smart contract	Four types of smart contracts	One type of smart contract
Performance analysis	Impact of transaction size (kB) on transaction response times	Throughput and the impact of data size (tps) on response time

The transaction response time is a time interval from a client sending a request to receiving a response, which is the sum of latency and service time. The response time is the main key performance indicators (KPIs) to evaluate the performance of the blockchain network (Nasir et al., 2018). Three kinds of transaction time are selected to provide a comprehensive evaluation, including hash creation time, upload transaction to block via IoT devices, and MSP approval transaction time by REST API.

Fig. 9 presents a polar graph of each transaction's total time under ten different transaction sizes, ranging from 5 kB to 400 kB. This range is supported by all transactions which are happened in the blockchain network with considering on-chain protocol. It demonstrates the trend that the total time increases with the transaction sizes. Moreover, the increasing rate enlarges when the total transaction size is over 200 KB, which provides insights for block size configuration to enable a blockchain platform with high performance.

Table 6 presents results of transaction time in three stages. The transaction time are represented by the Mean, standard deviations (SD) and coefficient of variation (CV) based on the experiments. To provide a better visualized trend analysis, Fig. 10 is presented to illustrate block generation time under different transaction sizes. Three key findings could be discovered as follows:

- *The time of transaction is directly related to the size of transaction.* A larger transaction implies a longer processing time to create the transaction on the board, sending data about the communication network and processing the transaction between the validating nodes. The results show that transaction size influences the standard deviations of times, which generate a greater impact on upload

Table 4
The qualitative comparisons with the existing traceability platform.

Characteristics	Traceability platform				
	IoT-based centralized traceability (Oztekin et al., 2010; Urbano et al., 2020)	IoT-based distributed traceability (Alfian et al., 2020; Lomotey et al., 2017)	Cloud-based traceability (Qian et al., 2018)	Blockchain-based traceability (Li et al., 2019)	Proposed BIoT^3 platform
Scalability		✓	✓	✓	✓
Privacy	✓	✓	✓		✓
Ubiquitous access			✓	✓	✓
Authenticity				✓	✓
Sharing		✓		✓	✓
Interoperability		✓		✓	✓
Decentralization				✓	✓
Flexibility			✓	✓	✓
Security	✓		✓		✓
Transparency				✓	✓

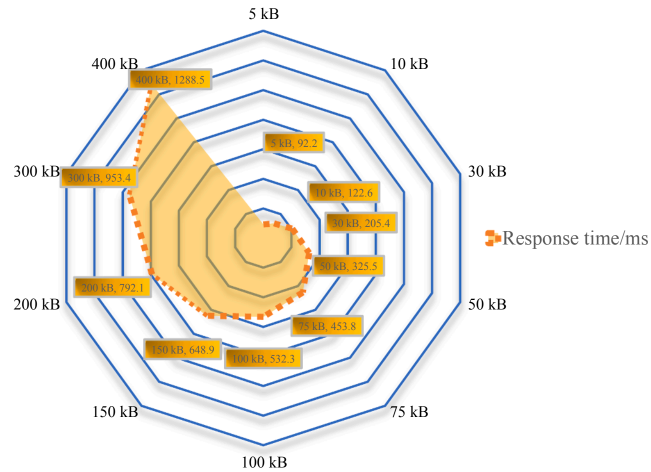

Fig. 9. Total response time for different transaction sizes.

transaction to block time and acceptance transaction time by RestAPI.

- *Standard deviation is only small in creation time but significantly high in upload time and MSP approval time.* Because the process of Creation is only related to hash generation, but standard deviation of Upload time is is related to collisions and packet losses in packet forwarding on an IP-based network. Also, standard deviation of MSP is related to consensus and membership verification in the blockchain network.
- *Standard deviation of transaction size 300 and 400 (kB) are quite high.* It makes the proposed approach unstable mainly for transaction size greater than 200 kB. For transaction size greater than 200 kB, each time an operation is performed, it will result in a high degree of unpredictability for the completion of the requested operation. Therefore, the block size could be set as 200 kB to guarantee a stable and high-performance blockchain platform.

5.5. Discussions and implications

Based on the experimental results and key findings, we summarize the main three implications from managerial, practical, and research perspectives, which are useful when various users making traceability decisions under blockchain-based drug supply chain.

Table 6
Results of transaction time in three stages.

Transaction Size(kB)	Creation			Upload			MSP approval		
	Mean(ms)	SD(ms)	CV(%)	Mean(ms)	SD(ms)	CV(%)	Mean(ms)	SD(ms)	CV(%)
5	27.8	0.39	1.29	29.2	1.9	6.5	35.2	2.4	6.81
10	29.2	0.42	1.43	35.3	2.5	7	58.1	4.1	7.05
30	35.1	0.56	1.59	48.1	3.2	7.06	122.2	8.7	7.11
50	49.2	0.8	1.62	88.2	6.4	7.25	188.1	13.5	7.17
75	59.4	1.03	1.73	130.3	9.8	7.52	264.1	19.5	7.38
100	68.3	1.1	1.61	167.2	13.2	7.89	296.8	22.9	7.71
150	73.1	1.25	1.7	217.6	17.2	7.9	358.2	28.1	7.84
200	82.4	1.68	2.03	268.2	21.4	7.97	441.5	35.7	8.08
300	99.2	3.1	3.12	331.4	37.5	11.31	522.8	59.8	11.43
400	170.5	7.4	4.34	428.1	51.9	12.12	689.9	84.4	12.23

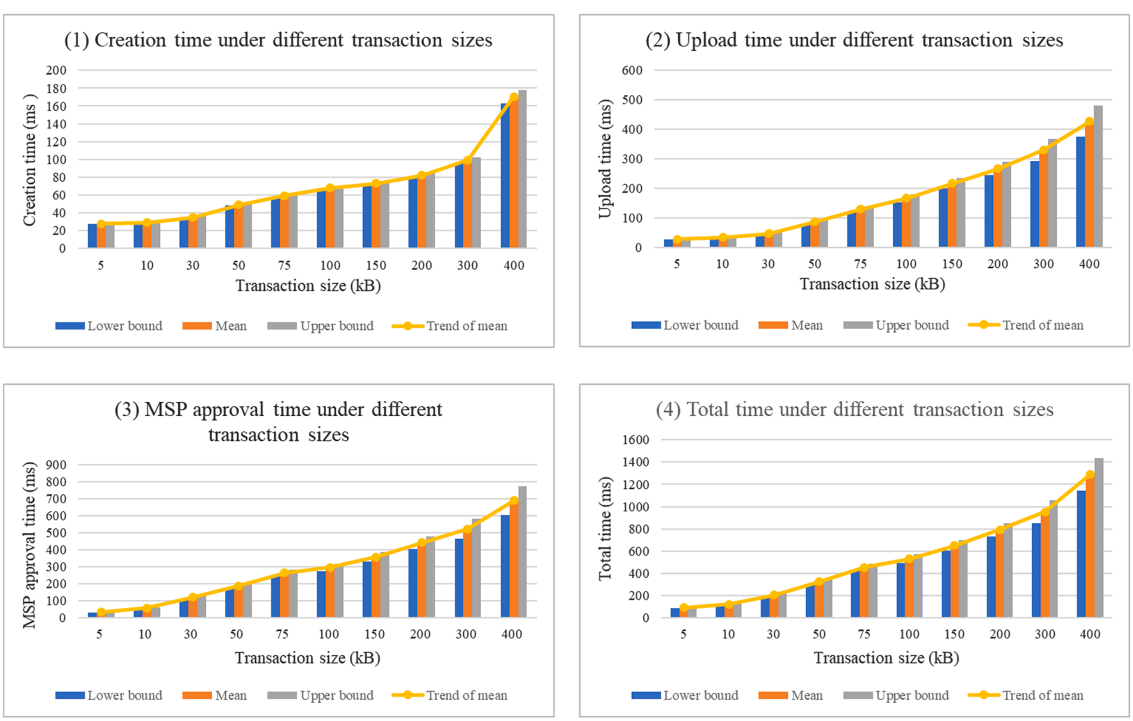

Fig. 10. Block generation time under different transaction sizes.

From a research perspective, this paper analyzes the performances of the proposed BIoT^3 platform from qualitative and quantitative comparisons. The qualitative comparison illustrates the advantages of the BIoT^3 platform over the existing traceability platforms, while the quantitative comparison highlights the difference between the BIoT^3 platform and the BCUM platform. Unlike previous throughput and latency analyses, the performance analysis of this paper focuses on exploring suitable block sizes to maximize the efficiency of the blockchain network. According to Fig. 10 (4), the results show that the optimal performance is achieved when the block size is configured as 200 kB with a response time of 792.1 ms. After that, with the increase of block size, the response time increases tremendously, which is not an efficient way to run the blockchain network.

From a practical perspective, this paper explores a roadmap for blockchain design, development, and application in the drug supply chain. Compared with previous literature, this paper explores the feasibility of blockchain-based on the collaborating company's data. Firstly, smart contract-enabled services facilitate product traceability, quality regulation, and risk analytics through the frontend interfaces. Moreover, this paper evaluates the efficiency of the blockchain network based on Hyperledger Fabric. It could provide some guidelines for further drug blockchain and smart contract implementations. Finally, the principle of on-chain and off-chain in the drug supply chain is built to guarantee necessary transparency and keep the privacy of off-chain data. For instance, according to the principle, the quality-related drug information, such as raw material quality information, GMP certificate, etc., needs to put on-chain for every consumer to access. The sensitive manufacturing process information in drug production is stored in the off-chain while its hash values store on-chain.

From a managerial perspective, the proposed BIoT^3 platform could achieve a transparent, secured, and trackable drug supply chain through the feasibility analysis. It is suggested that industrial managers should put more effort into blockchain-based workflow and functional design in further applications. For instance, the blockchain-based collaboration and incentive mechanisms are worthy of exploring both inside and outside the drug companies. It can enrich the blockchain-based functions for discovering more business opportunities.

6. Conclusion

This paper introduces a blockchain-based smart tracking and tracing platform to achieve a transparent, secured, and integrated drug supply chain. Firstly, a unified five-layer blockchain architecture is systematically designed to track and trace drug production, logistics, sales, and usage. Secondly, an on-chain and off-chain standard is built to determine whether the drug data is put on-chain or off-chain storage. It provides a practical method to guarantees the blockchain network performance in data storage and meets the data privacy requirements of the drug stakeholders. Thirdly, smart contract-enabled alert mechanism is designed and developed, which could provide a consistent solution from drug production to usage for solving the fake/poor-quality drugs issues. Finally, this paper explores the use of Hyperledger Fabric to evaluate the feasibility and efficiency of the blockchain platform. The results show that the proposed platform can provide more traceable and transparent drug trails.

The main contributions of this paper can be summarized as follows: (1) This paper proposes a blockchain-based smart tracking and tracing platform for the drug supply chain. An IoT-based four-level traceability approach is designed for drug identity recognition and management, including item-level, box-level, pallet-level, and truck-level. It not only helps to gain multi-tier traceability and visibility into the drug supply chain, but also establishes a transparent supply chain environment for drug collaborating participants. (2) This paper presents a practical roadmap for drug stakeholders to develop, implement, and evaluate their blockchain-based solutions. Specifically, blockchain-based R&D considerations provide the drug practitioners the insights, including the selection of blockchain architecture types, the principle of data on-chain and off-chain, and integration with external systems. The performance of the blockchain-based platform has been evaluated. The results show that the transaction size should be no greater than 200 kB to achieve optimal performance. (3) Smart contract-based alert mechanisms are built to detect and resolve potential issues. Based on the smart alert service in the case study, the drug stakeholders and consumers could quickly get the drug quality information and identify the potential counterfeit drug. It is important to guarantee a safe and transparent drug supply chain and public health.

The limitations and future improvements could be extended from the practical, technological, and organizational perspectives. From a practical perspective, it is necessary to apply the proposed BIoT^3 platform in the drug supply chain. Because complex operational processes and interest-conflicting users exist in real scenarios, the practicability needs to be verified in collaborating companies. From a technological perspective, this paper only considers limited stakeholders to test the efficiency of the proposed platform. The larger stakeholders' scale with more devices is worthy of exploring to verify its practicability. From an organizational perspective, more value metrics need to be considered to measure actual benefits and risks from the final deployed BIoT^3 solution, such as the return on investment and user experiences, etc. For instance, under the real application of blockchain solutions, the users' feedbacks are necessary to collect through the pilot study to optimize the blockchain-based traceability workflow.

CRediT authorship contribution statement

Xinlai Liu: Writing - original draft, Conceptualization, Investigation, Methodology. **Ali Vatankhah Barenji:** Writing - Original draft revision, Formal analysis. **Zhi Li:** Supervision, Project administration, Writing - reviewing and editing. **Benoit Montreuil:** Supervision, Writing - reviewing and editing. **George Q. Huang:** Supervision, Writing - reviewing and editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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