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Agility of the Drug Supply Chain Considering Economic and Social Aspects: Use of Internet of Things and Big Data Analysis

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ABSTRACT

The importance of drug supply and the efficiency and effectiveness of the drug supply chain as a strategic commodity are not embedded in many economic analyses. Supplying raw materials for the production, storage, and distribution of medicines within a supply chain network is crucial. Today, the development of the Internet of Things and the analysis of vast amounts of data have enabled the rapid preparation of large data production resources, allowing decisions in the drug supply chain network to be made quickly with the aid of appropriate tools. This article aims to provide a framework for agile drug supply chain management, focusing on the Internet of Things and big data analysis to manage the country's drug supply chain effectively. Rebif-22-44 drugs, which are used in the treatment of MS disease, are investigated in this paper, and an attempt is made to minimize the costs of the drug supply chain network design and minimize the maximum unmet demand of drug distribution based on big data sources by using a framework. MOGWO analysis tools and epsilon constraints are discussed. Considering the existence of uncertainty in drug demand and transportation costs, the robust possibilistic planning method has been used to control uncertain parameters. The analysis of big data shows that, in order to reduce the shortage of drugs in the country, it is necessary to use more supplies and increase the number of drug production centers and warehouses. This leads to an increase in the design costs of the supply chain network. In the analysis of the model, 11 efficient solutions were obtained by the MOGWO algorithm, and seven efficient solutions were obtained by the epsilon constraint method. It was also observed that, in Iran, with the increase in the uncertainty rate, the demand for Rebif-22-44 drugs has increased, and this has led to a rise in network design costs and drug shortages in the country. Concretely, lowering the maximum unmet demand from 78 to 47 units required raising the total network cost from 1,303,212.72 to 1,498,842.94 (USD), quantifying the cost-equity trade-off, and MOGWO produced a broader, faster Pareto set than the ϵ -constraint method (11 solutions in 68.49 s, MSI = 195,630 vs. seven solutions in 1,342.15 s, MSI = 184.4).

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1. Introduction

Commercial and industrial organizations around the world are exposed to severe instability arising from environmental disruptions [1], and the pharmaceutical industry is no exception. The pharmaceutical industry is constantly changing and evolving. The opportunities and threats in this industry encompass factors such as wars, various diseases, and technological advancements in discovering new pharmaceutical molecules, which have created a dynamic environment in this sector. In addition, an annual turnover of more than one trillion dollars has made this industry highly competitive, especially in the areas of developing new drugs, quality-based products, and high efficiency [2]. The pharmaceutical services sector is vital in all countries for two reasons. First, it deals with human life, and in all societies, human capital is one of the most fundamental assets a country possesses. Second, because of the high financial turnover in this industry, it is of great importance [3]. In recent years, the issue of medicines and their supply has become one of the world's important and challenging topics [4].

The pharmaceutical supply chain (PSC) plays a vital role in the health system of society and has been one of the most important goals of the health system in every country. Customers and governments demand better performance in drug distribution and service delivery in the best possible way, and in the shortest time and at the lowest cost, which underscores the importance of pharmaceutical SC management [5]. Uncertainty in the magnitude of changes and fluctuations across different parts of the SC, arising from demand volatility, financial conditions, technological changes, natural events, and so on—has compelled organizations to allocate resources to address such uncertainties so that, on the one hand, they can reduce volatility through solutions such as forecasting and preparedness and, on the other hand, improve the SC [5]. Within the complex fabric of the pharmaceutical industry, the SC acts as the backbone, orchestrating the production, distribution, and delivery of life-saving medicines. This network faces numerous challenges, including SC disruptions, counterfeit products, drug shortages, regulatory complexities, and more. The most challenging issue in the pharmaceutical SC is responding rapidly and agilely to customer needs (including clinics, hospitals, and individuals) based on accurate demand [6]. SC agility and flexibility refer to the ability of SC partner organizations to adapt quickly to fluctuations in their business environments [7]. Improving SC agility and flexibility are highly effective methods for strengthening firms' competitiveness. Agility in the pharmaceutical SC requires provisioning big-data sources using Internet-of-Things tools [8].

With the advent of Industry 4.0, SC have undergone fundamental changes that have profoundly affected production and procurement processes across various industries [9]. The term "Internet of Things (IoT)" refers to a set of technologies and research domains that enable global connectivity through physical objects around the world. Objects in the IoT can sense their surroundings, transmit data, and interact with one another [10]. The IoT is growing exponentially year by year, with targets such as smart homes and cities, e-health, and distributed information, among others [11]. The rapid evolution of the IoT has enabled seamless connectivity among devices and systems, transforming various industries and yielding significant advances in efficiency, productivity, and innovation. Through IoT, sectors such as healthcare, manufacturing, transportation, and smart cities have been able to deploy interconnected devices that monitor, analyze, and automate tasks, creating a more responsive and data-driven operating environment [12].

The multiple capabilities offered by the IoT have extended into previously unanticipated domains, such as human health and physiological monitoring. IoT enables real-time monitoring and improved inventory management, and artificial intelligence supports demand forecasting and anomaly detection [13]. Collectively, these advances enhance SC operations, providing superior efficiency and

accuracy, reduced operating costs, improved traceability, and greater scalability [14]. Smart healthcare and predictive maintenance in industries that incorporate aspects of the IoT are examples of domains that seek rapid and accurate outcomes [15]. In the literature, applications of IoT in key areas of the SC, including inventory management, asset tracking, cold-chain monitoring, predictive maintenance, route optimization, and waste reduction, have been discussed [16].

The integration of artificial intelligence (AI) with the IoT represents a significant advancement in pharmaceutical manufacturing and effectively bridges the gap between the digital and physical worlds. By embedding AI algorithms into IoT sensors, improvements are achieved in the manufacturing process and quality control, resulting in enhanced overall efficiency [17]. In Iran, given the uncertainty in the magnitude of medicine demand, collecting the required market data is not readily feasible, and modern technologies must be used for this purpose. Suppliers can make better decisions about how to procure pharmaceutical raw materials, distribution centers about production levels, and warehouses about the amount of medicine to store according to societal needs. Therefore, managing such a problem requires an agile framework for the pharmaceutical SC based on the IoT and big data analytics [18]. Additionally, designing a model for provisioning massive data-generation resources to the country's pharmaceutical industry is another existing gap in Iran's pharmaceutical sector.

Given the importance of this topic, a pharmaceutical SC network model was designed in this study with the objectives of minimizing the total costs of network design and minimizing the maximum unmet demand. The data required for this model are collected via IoT tools and analyzed in an advanced information system within a database. The analyzed big data (BD) are employed, based on the MOGWO algorithm and the epsilon-constraint method [19, 20], to optimize the country's pharmaceutical SC network. Considering the uncertainty in the demand for Rebif 22–44—used in the treatment of MS in the country—a robust stochastic programming approach was used to control the model. The output of the proposed framework in this model includes the selection of effective suppliers, the determination of optimal locations for distribution centers and warehouses, the calculation of the storage capacity for medicines produced in warehouses, and the optimal allocation of medicines across all tiers of the pharmaceutical SC network.

2. Research Background

The importance of designing drug SC networks, combined with the use of the IoT and BD analysis, has led many researchers to develop numerous frameworks and mathematical models. They have utilized various analytical methods and tools to optimize the drug's stability and employed BD analysis to enhance the drug's stability. Alotaibi *et al.*, [21] provided an overview of the use of BD in the healthcare SC. They explored various concepts related to this topic, including BD, BD analytics, and the role of BD in healthcare and healthcare SC management. The results demonstrated that the application of BD in healthcare SCs holds significant potential and warrants further investigation. Burns *et al.*, [22] examined the process of setting key parameters. Their approach is based on BD analysis and simulation using system dynamics theory and Vensim software modeling to optimize system performance. This study proposes a theoretical framework for problem-solving. Chamekh *et al.*, [23] proposed a context-aware middleware for an RFID-based pharmacy SC with the aim of providing deeper intelligence for object monitoring. Finally, a variant of Fosstrack middleware was proposed to provide deeper intelligence in the RFID-based SC. Montoya *et al.*, [24] highlighted the potential use of IoT features, considering the risk management approach in the PSC and based on an exploratory research method.

Shafiq *et al.*, [25] experimentally examined the relationship between the adoption of BD Predictive Analytics (BDPA), the adoption of Radio Frequency Identification (RFID), and SC performance. They considered the population of this paper as the pharmaceutical logistics industry in China. Data were collected through an adapted questionnaire, and Smart PLS 3.0 software was used to analyze the structural equation model. The results showed that for SC managers in the pharmaceutical industry, adopting and implementing BDPA and RFID technology would be beneficial in increasing SCP. Ben Daya *et al.*, [26] examined the role of the IoT and its impact on supply chain management (SCM) through an extensive literature review based on methodology, industry sector, and focusing on classification based on chain processes and central supply. The results showed that most studies have focused on conceptualizing the impact of the IoT, with limited analytical models and empirical studies, as well as on the delivery SC process and the food and production SC. They also identified areas of future SCM research that could support IoT implementation. Botcha *et al.*, [27] proposed an approach to increase traceability in the PSC using the IoT and blockchain. The results showed that blockchain ensures traceability, which helps improve industry efficiency by providing consumer protection, building trust, and enhancing service quality.

Namdej *et al.*, [28] conducted a study with the aim of discovering the effects of adoption, routinization, and absorption of BD on environmental performance. They critically analyzed past research and data, deriving hypotheses. Validation was done through a survey and data collection from the Thai pharmaceutical industry, and the data were analyzed using SPSS and AMOS. The results showed that the effect of BD acceptance on environmental performance is insignificant, the effect of BD routinization on environmental performance is significant, and the impact of BD assimilation on environmental performance is also significant. Pall *et al.*, [29] investigated the application of BD analysis in the reservation process in ordering drug stocks in large pharmacies, so that they can speed up the process of ordering drug stock. They collected data using BD analysis and the survey method. Sharma *et al.*, [30] reviewed the potential applications of the IoT in drug production, warehousing, and SCM to increase product quality, increase productivity, and reduce errors in different stages of a pharmaceutical product. The results showed that the IoT is helpful in monitoring and optimizing the operations of various units, enabling real-time monitoring and control, thereby increasing production efficiency. Premkumar *et al.*, [31] conducted a thorough review of the development in healthcare related to the pharmaceutical industry, focusing on the implementation of blockchain and the IoT. This analysis included domain applications, future analysis, and challenges associated with this plan.

Singh *et al.*, [32] proposed an IoT-based sensor framework for blockchain in their research, which tracks drugs as they slowly pass through the entire SC. Their primary focus was on enhancing classical blockchain systems to make them more suitable for IoT-based SCM, as the adoption of these technologies promises to enable a viable smart health ecosystem throughout the PSC. Safkhani *et al.*, [33] evaluated the security level of a recently proposed protocol and proved its vulnerabilities due to the lack of complexity in bitwise functions. They presented an improved lightweight protocol based on authenticated cryptosystems (AE). The results of the security analysis showed that the weaknesses of the previous efforts were all adequately addressed. Additionally, the improved protocol boasts a robust security posture in terms of confidentiality and integrity. Rejeb *et al.*, [34] investigated the IoT in SCM and logistics. They analyzed 807 articles from published journals and then evaluated them according to bibliometric parameters, including year of publication, number of references, authors, and institutions. Pesqueira *et al.*, [35] presented an article with the aim of investigating the extent of development in BD technology and data-related processes, as well as the different professional skills and competencies in the healthcare and pharmaceutical industries, with the goal of creating sustainable development to address organizational challenges. This study

provided an in-depth examination of how BD technology and processes currently impact the healthcare and pharmaceutical industries.

Shams Al-Zoha *et al.*, [36] conducted commissioned research aimed at investigating how a centralized logistics system minimizes travel costs and supports environmental sustainability for a Finnish pharmaceutical wholesaler. They employed a mixed-methods research approach, combining quantitative and qualitative data. The results showed that a centralized pipeline system can provide improved information flow, higher transport capacity, and reduced CO₂ emissions, supporting environmentally friendly and sustainable SC and logistics processes. Ahmadi *et al.*, [18] investigated new pharmaceutical governance based on IoT and blockchain technology in a study. They concluded that implementing an IoT-based blockchain system provides the tools to improve the pharmaceutical industry's management along the SC, thereby making healthcare more efficient and reliable. Hussain *et al.*, [37] investigated blockchain-based IoT developments and their current use. They discussed the smart devices used in this system and which device is most suitable in the SC. They also explored future themes in the blockchain-based IoT, which is referred to as an executive framework production network. Zahedi *et al.*, [38] used two innovative approaches (prioritization and allocation) to design an aid SC network using the IoT to handle suspicious cases during an epidemic such as SARS-CoV-2. They examined each approach using several test problems and a real case in Iran. A set of meta-heuristic and hybrid algorithms was developed to optimize the proposed models. The proposed methods have demonstrated their versatility in various situations related to the SARS-CoV-2 pandemic.

Tyagi *et al.*, [39] studied the impact of Big Data Analytics (BDA) on healthcare SC innovation, SC responsiveness, and SC flexibility under the moderating effect of innovation leadership in the context of the COVID-19 pandemic. They tested the hypotheses using data collected from 190 respondents in the healthcare industry. Structural equation modeling analysis using the Partial Least Squares (PLS) method revealed that BDA capabilities play a crucial role in creating a responsive HSC and enhancing innovation. Rayan *et al.*, [40] investigated counterfeit drugs and the innovative management of the drug SC safely through an integrated blockchain framework of the IoT. The results showed that the adoption of this framework improves the management of drugs in the drug SC, thereby providing better healthcare services. Goodarzian *et al.*, [41] designed a green drug SC network under uncertainty. Their main objective was to create a fuzzy bi-objective Mixed Integer Linear Programming (MILP) model for a multi-period, three-level, multi-product, and multi-modal transport Green Medicine SC Network (GMSCN) and to investigate the environmental effects related to the establishment of pharmacies and hospitals. They used meta-heuristic algorithms to solve the model. They developed two firefly and simulated annealing algorithms (HFFA-SA) and a hybrid firefly and social engineering optimization algorithm (HFFA-SEO) to solve the proposed model. The results showed that the GMSCN model and the developed solution approaches are promising.

Ali Ahmadi *et al.*, [42] investigated the dimensions and key components of the use of BD obtained from the IoT in the SC of an industry. They presented a model for implementing an agile and lean SC based on IoT data analysis to improve SC performance in critical situations. The results showed that these technologies can be used as a powerful agent, especially in the distribution of fast-acting pharmaceutical products. Delfani *et al.*, [43] presented a new location-allocation-inventory model as a multi-objective, multi-level, multi-product, multi-period, and multi-modal transport system for designing a PSC network under uncertainty in their research. The proposed model aimed to minimize the total cost and delivery time while simultaneously maximizing the reliability of the transportation system. They used Red Deer Algorithms (RDA) in its multi-objective form, abbreviated as IMORDA,

and (NSGA-II) and (MOPSO) algorithms. The results confirmed the applicability and efficiency of IMORDA for the proposed model.

A study examined the impact of the IoT and BDA on SC visibility (SCV) and operational performance (OP) in pharmaceutical manufacturing. Drawing on a literature-based conceptual model, the findings showed that both IoT and BDA exert positive, statistically significant effects on SCV and OP. SCV was likewise positively and significantly related to OP. Mediation analyses further confirmed that SCV transmits part of the impact of IoT and BDA to OP, i.e., SCV acts as a mediator in these relationships [44]. A study proposed a risk-management framework to identify significant risk factors in the PSC. It employed fuzzy failure mode and effects analysis (FMEA) and Data Envelopment Analysis (DEA) to assess risk exposure. A Malaysian case study indicated that the pharmacy node was the most vulnerable link. The most critical risks involved the unavailability of medicine due to unexpected demand and the scarcity of specialty or substitute drugs. These risks were considered mitigable through the use of digital technologies. The authors proposed a digital platform that integrates BDA and blockchain to address supply shortages [45]. A study proposed and developed an integrated, multi-period, multi-objective model for the medicine SC in healthcare. It was considered a two-echelon setting with fuzzy inventory for pharmaceutical products. The work began by formulating a mathematical model centered on the business triad of time, quality, and cost. Then it introduced a modified interactive multi-objective fuzzy programming approach to optimize this triad. The method fused expert judgment using fuzzy linguistic variables with triangular membership functions, and a numerical example demonstrated its practical applicability [46].

A study introduced a comprehensive framework that integrates quality, sustainability, and agility in pharmaceutical manufacturing. Using data from automated (online) inspection systems, the framework elevated product quality, enabled preventive maintenance planning, and optimized production scheduling. The authors developed an Integrated Quality–Maintenance–Production (IQMP) model grounded in Bayesian methods. Results showed that IQMP enhances product quality, stabilizes operations, and increases agility in the face of environmental changes and operational variability. Incorporating streaming inspection data markedly improved the accuracy and efficiency of decisions related to quality control, maintenance, and production planning [47]. A study proposed a multi-echelon PSC Network (PSCN) built on BDA in the context of the COVID-19 pandemic. The authors formulated a new Mixed-Integer Non-Linear Programming (MINLP) model that jointly handles allocation, production planning, and inventory control—termed the LAPI problem. They then linearized the formulation via a transformation procedure to obtain a tractable model. The optimization sought to (i) minimize total system cost and transportation-related CO₂ emissions and facility setup impacts, while (ii) maximizing medicines' shelf life. Demand for essential drugs was estimated through simulation, highlighting the model's practical relevance and effectiveness in real-world settings [48]. A study formulated a multi-objective model for PSC optimization that simultaneously minimized total cost and environmental impact while maximizing service-level equity (i.e., the minimum service-level ratio). It also developed a disruption model and compared its performance with a baseline. Results illustrated objective-driven behavior: cost minimization tended to maximize capacity utilization; environmental goals reduced production levels to satisfy coverage requirements; and maximizing the minimum ratio expanded the number of facilities. An epsilon-constraint analysis revealed trade-offs in which the environmental budget constrained flexibility between the attainable total cost and the minimum service-level ratio [49].

A study developed a novel Mixed-Integer Non-Linear Programming (MINLP) formulation for joint allocation, production planning, and inventory control—the LAPI problem. It linearized the model via a transformation procedure to improve computational efficiency. The formulation aimed to minimize

total costs, transportation-related CO₂ emissions, and facility-establishment impacts while maximizing the shelf life of medicines. Computational experiments showed that medium- and large-scale instances—characterized by BDA's three V's (variety, velocity, and volume)—were challenging for exact optimization. A simulation approach was used to estimate demand for required pharmaceuticals [48]. A paper proposed an efficient, secure IoT–cloud–blockchain system for PSC management (SCM) automation and analytics. It leveraged a hierarchical IoT–Mist–Edge–Fog–Cloud (IMEFC) architecture to enhance Communication, Response, Compute, Security, and Storage (CRCSS). Blockchain safeguards SCM transactions and data. Efficiency was evaluated via upload/download time and transaction fees on Bitcoin, Ethereum, and Filecoin. Filecoin performed faster and more cost-effectively for larger files than Ethereum and Bitcoin, making it suitable for pharmaceutical SCM [50].

A study formulated a mathematical model for a perishable medical-goods SC under uncertainty. It was considered as a three-echelon network, comprising suppliers, intermediate warehouses, and end customers, where customer service demand and warehouse sojourn times follow exponential distributions. The model sought to minimize total supply-chain cost and the total presence time of perishable items across the network. An LP-metric approach was used for small instances, while, due to NP-hardness, modified MOPSO and NSGA-II were applied to larger cases. Results indicated that these metaheuristics efficiently produced near-optimal solutions for large-scale problems within a reasonable time [51]. A study proposed a multi-objective model for locating fixed and mobile blood donation centers. The first objective minimized facility setup and transportation costs, while the second maximized quality by ensuring timely deliveries and satisfying hospitals' blood demand. The model utilized real-world urban traffic and donation data to evaluate its practical performance. An ϵ -constraint method optimized both objectives jointly. Scenario analyses optimized cost and quality separately, and the solution procedure identified effective center locations to meet demand. The formulation also accounted for quality-degrading factors, such as delayed deliveries and product returns, and demonstrated that these issues could be mitigated [52].

A study designed a data-driven, sustainable, resilient, and digitalized PSC network. It identified delivery time, quality, backup suppliers, robustness, and cost as the most influential indicators. The mathematical framework selected a blockchain-based platform to establish the Information-Sharing System (ISS) and assessed effectiveness by comparison with traditional methods. In the first stage, potential suppliers were evaluated using a Random Forest Regressor (RFR). A subsequent mathematical model configured the PSC with explicit resilience and sustainability features, and a Fuzzy Lexicographic Multi-Choice Archimedean–Chebyshev Goal Programming (FLMCACGP) approach was employed to obtain the optimal solution [53]. A study investigated a bi-objective medical SC design problem under pandemic-induced ripple-effect uncertainty. It formulated a generic bi-objective robust optimization model to capture the propagation of disruptions and parameter volatility mathematically. It instantiated the model using a real Turkish case and generated scenario sets that reflected simultaneous drops in capacity utilization rates and surges in product demand. It employed the improved augmented ϵ -constraint method (AUGMECON2) to obtain a diversified set of Pareto-optimal solutions that mapped the trade-offs between the two conflicting objectives. It further analyzed the resulting Pareto sets with multiple comparison metrics to assess solution diversity, distribution, and quality from complementary perspectives. It concluded that a unified mitigation strategy enhanced MSC resiliency across a wide range of disruption scenarios [54]. A study developed a multi-channel PDC differential game involving a manufacturer, a traditional retailer, and an e-commerce platform. It examined manufacturers' online-channel choices and the effects of introducing blockchain on operational policies, including pricing rules and quality assurance

processes. It validated the framework with numerical examples and MATLAB simulations. Results showed that the consumer out-of-pocket share and the preference for online purchasing jointly shaped the manufacturer's optimal online-sales arrangement: when either the out-of-pocket share or the online-channel preference was low, the manufacturer chose the reselling mode; conversely, it selected the agency mode. Introducing blockchain has improved both the retail price formation and the verifiable authenticity of pharmaceuticals, which has increased consumer trust, elevated perceived quality, stimulated demand, and raised the profitability of all supply-chain members. It also led manufacturers to invest more in quality assurance, supporting long-term business growth [55]. The results of a study showed that the five factors with the highest priority in the field of pharmaceutical services in Iran are, respectively: improving the quality of drug production, empowering medical personnel, enhancing the quality of drug distribution, promoting medical services for rare diseases, and improving the supervision of drug production. This study provided a structured approach to identify and prioritize the needs of patients with rare diseases in the Iranian pharmaceutical services system [3].

According to a background study of various research in the field of drug SC, with an emphasis on the IoT and BD analysis, it is observed that there is no specific framework for developing the agility of the drug SC in Iran. Due to the lack of a framework for preparing BD production resources and an agile SC framework based on large datasets in the pharmaceutical industry, this article attempts to address these issues. Therefore, the salient features of the article are stated as follows:

- i. Providing an agile SC framework based on BD in the pharmaceutical industry;
- ii. Presenting a model for providing the pharmaceutical industries with BD, with emphasis on the IoT and BD analysis;
- iii. Presenting a multi-objective mathematical model for the SCM of Rebif22-44 drugs in Iran;
- iv. Taking uncertainty into account and using the possibility-based planning method in data control;
- v. Using the MOGWO algorithm in the analysis of BD.

3. Providing a model for SCM in the pharmaceutical industry

The framework of agile SC based on BD in pharmaceutical industries, utilizing a 4-stage architecture of IoT (virtuality, market sensitivity, network-oriented, and process integration), is illustrated in Figure 1.

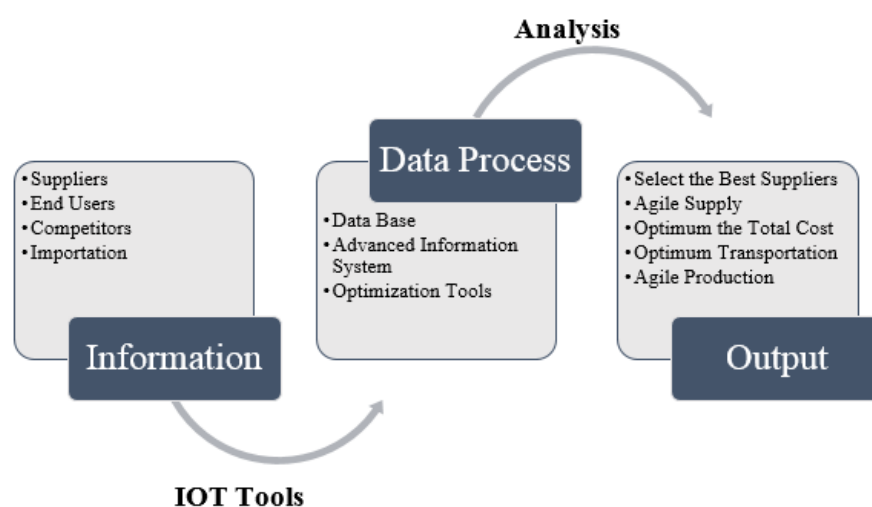


Fig. 1. Agile SC framework based on BD in the pharmaceutical industries (Source: Authors' illustration)

The first issue in using the stated framework is the possibility of extensive communication between the components of the SC, as well as the need for a technical platform and facilities to share information in real-time. Within this framework, all necessary information for the drug SC, including data from suppliers, final consumers, competitors, and drug imports, is collected and stored in a database utilizing IoT tools. BD stored in the database is analyzed using advanced information systems and optimization tools.

Since today, due to the existence of international sanctions, the reduction in the amount of medicine available in the country, and intense competition between drug-producing units, the effective use of the IoT and information networks has led to the adoption of software platforms by drug-producing units. This platform has enabled the collection of information from various levels of the drug SC network, including suppliers, the final market (such as hospitals and clinics), logistics, and other stakeholders. Intelligent agents and information technology have become a platform for the production and storage of BD in the SCM systems of the pharmaceutical industry, enabling communication between its various components. The different components of an SC in the pharmaceutical industry include suppliers, production centers, warehouses, and the final consumer, which is mostly hospitals and clinics, as shown in Figure 2.

In this form, a set of suppliers, utilizing data collected from IoT tools, provides the raw materials needed for drug production to manufacturers. Producers also decide on the amount of production and storage of drugs due to the fast perishability of drugs. After storing the drugs, they distribute the drugs based on the data collected from hospitals and clinics, using the IoT. Figure 2 is designed and validated according to the drug SC in Iran based on experts' opinions. The purpose of presenting this model is to optimize two different objective functions:

- i. Minimizing the costs of the entire drug SC network.
- ii. Minimizing the maximum unmet demand.

Information is collected and made available to all actors of the SC in the fastest time through IoT tools. However, there is a possibility of uncertainty in the drug SC network due to the occurrence of special conditions. Therefore, the presented mathematical model is based on uncertainty. The MOGWO algorithm, widely used in similar fields in the literature [56-58], has been employed to optimize BD information in this network. Additionally, the presence of uncertainty in the country's drug SC network has enabled the use of a robust planning method to control the uncertain parameters of demand and transportation costs.

The presentation of the mathematical model of the drug SC based on the IoT and BD is based on the following assumptions:

- i. Perishability of the drug from production to distribution is considered.
- ii. It is possible to transfer medicine between warehouses.
- iii. Customer demand is not fully met.
- iv. The demand parameter and transmission costs are considered non-deterministic.
- v. It is a multi-period, multi-product, and multi-level model.

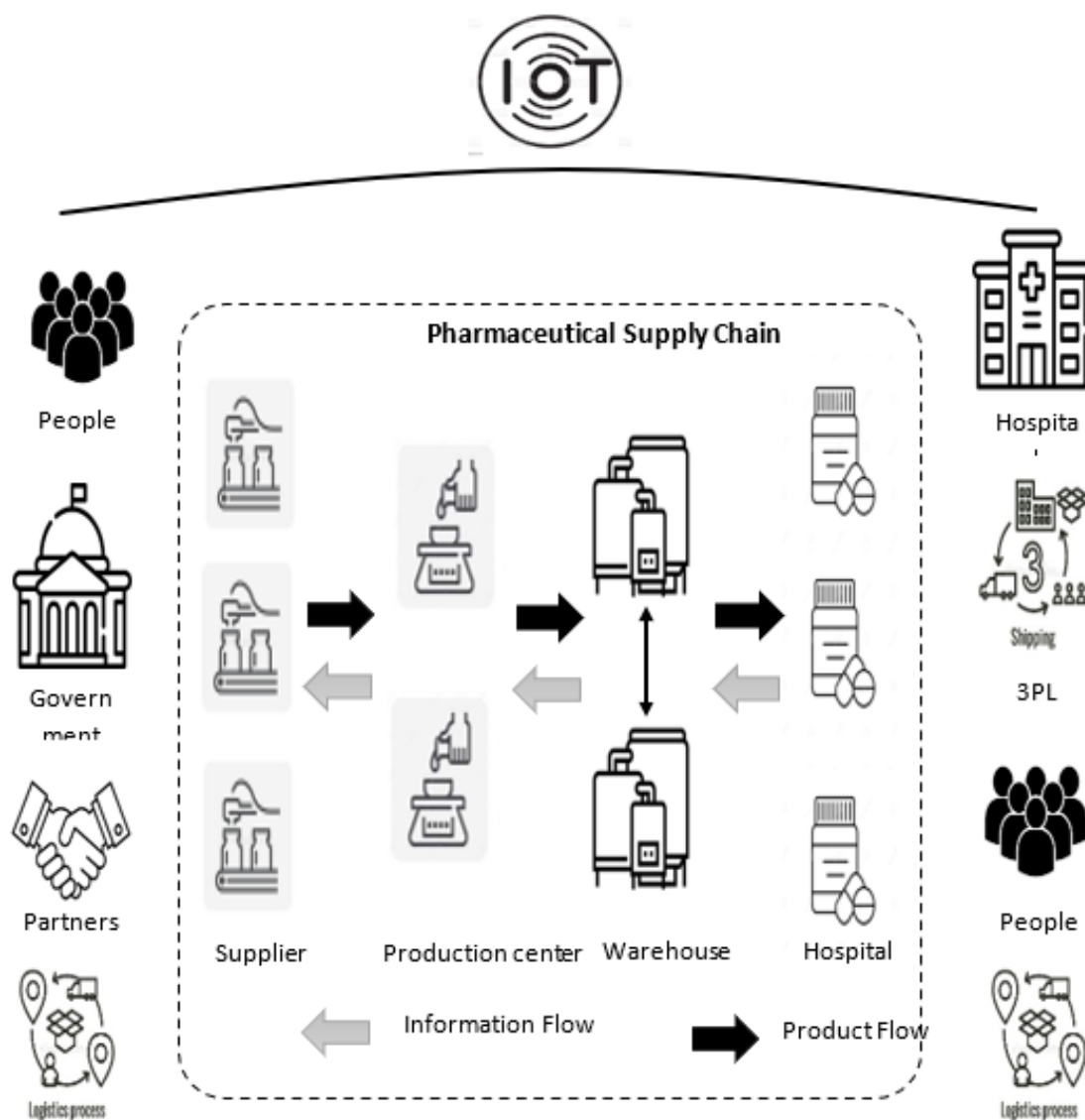


Fig. 2. Sources of BD production in the SC of the pharmaceutical industry (Source: Authors' illustration)

Based on the above assumptions and the mentioned objective functions (minimizing the costs of the entire drug SC network and minimizing the maximum unmet demand), the symbols used in the mathematical model are as follows.

Sets

I	A set of drug suppliers	$i \in \{1, 2, \dots, I\}$
J	A set of drug manufacturers	$j \in \{1, 2, \dots, J\}$
K	A set of drug storage warehouses	$k, k' \in \{1, 2, \dots, K\}$
H	Set of hospitals	$h \in \{1, 2, \dots, H\}$
P	Set of drugs	$p \in \{1, 2, \dots, P\}$
T	Set of time periods	$t \in \{1, 2, \dots, T\}$
R	A set of drug production courses	$r \in \{1, 2, \dots, T\}$
E	A set of drug delivery courses	$e \in \{1, 2, \dots, T\}$

Parameters

F_i	Supplier selection cost i
F_j	Fixed cost of production center j
F_k	Fixed warehouse cost k
H_j	Cost of drug storage in production center j
H_k	The cost of keeping medicine in the warehouse k
\widetilde{Tr}_{ij}	The cost of transporting a unit of medicine from supplier i to production center j
\widetilde{Tr}_{jk}	The cost of transporting a unit of medicine from production center j to warehouse k
$\widetilde{Tr}_{kk'}$	The cost of transporting a unit of medicine between warehouses k and k'
\widetilde{Tr}_{kh}	The cost of transporting one unit of medicine from warehouse k to hospital h
\widetilde{D}_{hpt}	Hospital h 's demand for drug p in time period t
v_p	Drug life cycle p
Cap_{ip}	The maximum capacity of supplier i of drug p
Cap_{jp}	The maximum capacity of production center j of drug p
Cap_{kp}	The maximum storage capacity k of medicine p
ss_{jpt}	Confidence inventory level of production center j of drug p in time period t
ss_{kpt}	Stock level of confidence warehouse k of drug p in time period t

Decision variables

X_{ijpt}	Amount of drug p transferred from supplier i to production center j in time period t
X_{jkpt}	The amount of drug p transferred from production center j to warehouse k in time period t
X_{khpt}	Amount of drug p transferred from warehouse k to hospital h in time period t
$X_{kk'pt}$	Amount of drug p transferred between warehouses k and k' in time period t
U_{jkprt}	The amount of drug p transferred in the time period t from the production center j to the warehouse k that was produced in the period r .
S_{khpret}	The amount of drug p transferred in time period t from retailer k to drug demand center h , produced in period r , and received in period e .
$V_{k'kpret}$	Amount of drug p transferred in time period t between warehouses k and k' produced in period r and received in period e .
In_{jptr}	The inventory level of drug p in the warehouse of production center j in time period t that is produced in period r .
In_{kptre}	Inventory level of drug p in time period t in warehouse k that was produced in period r and received in period e .
Y_i	If the supplier i is selected, it takes the value of 1, and otherwise it takes the value of 0
Y_j	If production center j is built, it takes the value of 1, and otherwise it takes the value of 0
Y_k	If warehouse k is built, it takes the value of 1, and otherwise it takes the value of 0

According to the defined symbols, the primary objectives of the mathematical model are to minimize the total costs of the entire drug SC network and minimize the maximum unmet demand, utilizing the BD collected through IoT tools and optimization tools. The most critical output results of the analysis of the model presented based on the framework of Figure 1 are the selection of potential suppliers, the optimal allocation of drug flow between the levels of the SC, and the determination of the optimal amount of drug stock in the warehouse.

According to the defined symbols as well as the analysis of the SC network of the country's pharmaceutical industry, the mathematical planning model of the drug SC network is as follows:

$$\text{Min } Z_1 = \sum_{i=1}^J F_i Y_i + \sum_{j=1}^J F_j Y_j + \sum_{k=1}^K F_k Y_k + \sum_{i=1}^I \sum_{j=1}^J \sum_{p=1}^P \sum_{t=1}^T \widetilde{T}r_{ij} X_{ijpt} + \quad (1)$$

$$\begin{aligned} & \sum_{j=1}^J \sum_{k=1}^K \sum_{p=1}^P \sum_{t=1}^T \widetilde{T}r_{jk} X_{jkpt} + \sum_{k=1}^K \sum_{h=1}^H \sum_{p=1}^P \sum_{t=1}^T \widetilde{T}r_{kh} X_{khpt} + \\ & \sum_{k=1}^K \sum_{k'=1}^K \sum_{p=1}^P \sum_{t=1}^T \widetilde{T}r_{kk'} X_{kk'pt} + \sum_{j=1}^J \sum_{p=1}^P \sum_{t=1}^T \sum_{r=1}^t H_j \text{In}_{jp\text{tr}} + \\ & \sum_{k=1}^K \sum_{p=1}^P \sum_{t=1}^T \sum_{e=r}^t \sum_{r=1}^t H_k \text{In}_{kp\text{tre}} \end{aligned} \quad (2)$$

$$\text{Min } Z_2 = \max_{h,p,t} \left\{ \widetilde{D}_{hpt} - \sum_{k=1}^K X_{khpt} \right\}$$

s. t.:

$$\sum_{r=1}^t \text{In}_{jp\text{tr}} = \sum_{i=1}^I X_{ijpt} - \sum_{k=1}^K X_{jkpt}, \quad \forall j, p, t = 1 < v_p \quad (3)$$

$$\sum_{r=1}^t \text{In}_{jp\text{tr}} = \sum_{r=1}^{t-1} \text{In}_{jp\text{tr}-1r} + \sum_{i=1}^I X_{ijpt} - \sum_{k=1}^K X_{jkpt}, \quad \forall j, p, 1 < t < v_p \quad (4)$$

$$\sum_{r=t+1-v_p}^t \text{In}_{jp\text{tr}} = \sum_{r=t+1-v_p}^{t-1} \text{In}_{jp\text{tr}-1r} + \sum_{i=1}^I X_{ijpt} - \sum_{k=1}^K X_{jkpt}, \quad \forall j, p, t \geq v_p \quad (5)$$

$$X_{jkpt} = \sum_{r=1}^t U_{jkprt}, \quad \forall j, k, p, t < v_p \quad (6)$$

$$X_{jkpt} = \sum_{r=t+1-v_p}^t U_{jkprt}, \quad \forall j, k, p, t \geq v_p \quad (7)$$

$$\text{In}_{jp\text{tr}} = \sum_{i=1}^I X_{ijpt} - \sum_{k=1}^K U_{jkprt}, \quad \forall j, p, r = t \quad (8)$$

$$\text{In}_{jp\text{tr}} = \text{In}_{jp\text{tr}-1r} - \sum_{k=1}^K U_{jkprt}, \quad \forall j, p, t - r < v_p \quad (9)$$

$$\sum_{e=r}^t \sum_{r=1}^t \text{In}_{kp\text{tre}} = \sum_{j=1}^J X_{jkpt} - \sum_{h=1}^H X_{khpt} + \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{k'kpt} - \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{kk'pt}, \quad \forall k, p, t = 1 < v_p \quad (10)$$

$$\sum_{e=r}^t \sum_{r=1}^t \text{In}_{kp\text{tre}} = \sum_{e=r}^{t-1} \sum_{r=1}^{t-1} \text{In}_{kp\text{tre}-1re} + \sum_{j=1}^J X_{jkpt} - \sum_{h=1}^H X_{khpt} + \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{k'kpt} - \quad (11)$$

$$\sum_{\substack{k'=1 \\ k \neq k'}}^K X_{kk'pt}, \quad \forall k, p, 1 < t < v_p$$

$$\sum_{e=r}^{r+v_p-1} \sum_{r=t-v_p+1}^t \ln_{kptre} = \sum_{e=r}^{t-1} \sum_{r=t-v_p+1}^{t-1} \ln_{kpt-1re} + \sum_{j=1}^J X_{jkpt} - \sum_{h=1}^H X_{khpt} + \quad (12)$$

$$\sum_{\substack{k'=1 \\ k \neq k'}}^K X_{k'kpt} - \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{kk'pt}, \quad \forall k, p, t \geq v_p$$

$$X_{khpt} = \sum_{e=r}^t \sum_{r=1}^t S_{khpret}, \quad \forall k, h, p, t < v_p \quad (13)$$

$$X_{khpt} = \sum_{e=r}^t \sum_{r=t-v_p+1}^t S_{khpret}, \quad \forall k, h, p, t \geq v_p \quad (14)$$

$$X_{k'kpt} = \sum_{e=r}^t \sum_{r=1}^t V_{k'kpret}, \quad \forall k, k', p, t < v_p \quad (15)$$

$$X_{k'kpt} = \sum_{e=r}^t \sum_{r=t-v_p+1}^t V_{k'kpret}, \quad \forall k, k', p, t \geq v_p \quad (16)$$

$$\ln_{kptre} = \sum_{j=1}^J U_{jkprt} - \sum_{h=1}^H S_{khpret} + \sum_{\substack{k'=1 \\ k \neq k'}}^K V_{k'kpret} - \sum_{\substack{k'=1 \\ k \neq k'}}^K V_{kk'pret}, \quad \forall k, p, r, e = t \quad (17)$$

$$\ln_{kptre} = \ln_{kpt-1re} - \sum_{h=1}^H S_{khpret} - \sum_{\substack{k'=1 \\ k \neq k'}}^K V_{kk'pret}, \quad \forall k, p, r, t - e < v_p \quad (18)$$

$$\sum_{j=1}^J X_{ijpt} \leq \text{Cap}_{ip} \cdot Y_i, \quad \forall i, p, t \quad (19)$$

$$\sum_{i=1}^I X_{ijpt} \leq \text{Cap}_{jp} \cdot Y_j, \quad \forall j, p, t \quad (20)$$

$$\sum_{j=1}^J X_{jkpt} + \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{k'kpt} \leq \text{Cap}_{kp} \cdot Y_k, \quad \forall k, p, t \quad (21)$$

$$\sum_{r=1}^t \ln_{jptr} \geq \text{ss}_{jpt} \cdot Y_j, \quad \forall j, p, t \quad (22)$$

$$\sum_{e=r}^t \sum_{r=1}^t H_k \ln_{kptre} \geq \text{ss}_{kpt} \cdot Y_k, \quad \forall k, p, t \quad (23)$$

$$\ln_{jptr} = 0, \quad \forall j, p, t < r \quad (24)$$

$$\ln_{kptre} = 0, \quad \forall k, p, e, t < r \quad (25)$$

$$In_{kptre} = 0, \quad \forall k, p, r, e < r \quad (26)$$

$$X_{ijpt}, X_{jkpt}, X_{khpt}, X_{kk'pt}, U_{jkprt}, S_{khpret}, V_{kk'pret}, In_{jptr}, In_{kptre} \geq 0, \quad \forall i, j, k, k', h, p, t, e, r \quad (27)$$

$$Y_i, Y_j, Y_k \in \{0,1\}, \quad \forall i, j, k \quad (28)$$

Equation (1) minimizes the costs of the entire drug SC network. These costs include the expenses of selecting and establishing a supplier, production center, and warehouses, as well as drug transfer costs between facilities and storage costs in the warehouse. Equation (2) seeks to minimize the maximum unmet demand from drug distribution to demand points such as hospitals. In this regard, the balance equation for the uniform distribution of medicine to all demand points has been included. The equations (3) to (5) calculate the accumulated level of the drug according to the time of perishability in a production facility for each time period. Equations (6) and (7) calculate the total flow of a drug from a manufacturing facility to a warehouse during the manufacturing period. The equations (8) and (9) determine the accumulated level of drug for a production center warehouse based on the time of the production cycle. Equations (10) to (12) show the inventory level of a warehouse for different time periods. Equations (13) to (16) determine the drug transfer flow between the warehouse and hospitals based on the time of the production period. The equations (17) and (18) calculate the stock level of a warehouse based on the time of the drug delivery period. Equation (19) to (21) shows the maximum capacity utilization of suppliers, production centers, and warehouses. Equations (22) and (23) guarantee that the amount of inventory at the end of the time period is greater than the level of confidence. Equations (24) to (26) show the logical relations in the mathematical model. Equations (27) and (28) specify the gender and type of decision-making variables.

Equation (2) in the above equation is a non-linear equation, and in order to linearize the model, you can replace equations (29) and (30) instead of equation (2):

$$\text{Min } Z_2 = \gamma \quad (29)$$

s. t.:

$$\gamma \geq \tilde{D}_{hpt} - \sum_{k=1}^K X_{khpt}, \quad \forall h, p, t \quad (30)$$

Due to the indeterminacy of the demand parameters and transportation costs, in this article, the robust possibility method is used to control the model parameters. Therefore, considering the collection of demand data through IoT tools and its analysis in the database using optimization tools, there is a possibility of uncertainty in the demand amount under certain conditions and transportation costs. Therefore, first, by using the opinions of experts, each of the non-deterministic parameters has been quantified in three levels of optimistic, probable, and pessimistic under triangular fuzzy numbers. Therefore, the first step in controlling the non-deterministic parameters of the problem is to use the fuzzy programming method and the influence of experts' opinions in maintaining the model. Based on this, each of the non-deterministic parameters of the model is converted into triangular fuzzy numbers as follows:

Parameter	Optimistic	Likely	Pessimistic
\tilde{Tr}_{ij}	Tr_{ij}^1	Tr_{ij}^2	Tr_{ij}^3
\tilde{Tr}_{jk}	Tr_{jk}^1	Tr_{jk}^2	Tr_{jk}^3
$\tilde{Tr}_{kk'}$	$Tr_{kk'}^1$	$Tr_{kk'}^2$	$Tr_{kk'}^3$
\tilde{Tr}_{kh}	Tr_{kh}^1	Tr_{kh}^2	Tr_{kh}^3
\tilde{D}_{hpt}	D_{hpt}^1	D_{hpt}^2	D_{hpt}^3

As a result, by using the fuzzy programming method and the following relations, triangular fuzzy numbers can be used instead of non-deterministic numbers in the above model. In these relationships, α , the uncertainty rate, is defined, and its range is [0.1, 0.9].

$$\begin{aligned} \text{Min } Z_1 = & \sum_{i=1}^J F_i Y_i + \sum_{j=1}^J F_j Y_j + \sum_{k=1}^K F_k Y_k + \\ & \sum_{i=1}^I \sum_{j=1}^J \sum_{p=1}^P \sum_{t=1}^T \left(\frac{\text{Tr}_{ij}^1 + 2\text{Tr}_{ij}^2 + \text{Tr}_{ij}^3}{4} \right) X_{ijpt} + \\ & \sum_{j=1}^J \sum_{k=1}^K \sum_{p=1}^P \sum_{t=1}^T \left(\frac{\text{Tr}_{jk}^1 + 2\text{Tr}_{jk}^2 + \text{Tr}_{jk}^3}{4} \right) X_{jkpt} + \\ & \sum_{k=1}^K \sum_{h=1}^H \sum_{p=1}^P \sum_{t=1}^T \left(\frac{\text{Tr}_{kh}^1 + 2\text{Tr}_{kh}^2 + \text{Tr}_{kh}^3}{4} \right) X_{khpt} + \\ & \sum_{k=1}^K \sum_{k'=1}^K \sum_{p=1}^P \sum_{t=1}^T \left(\frac{\text{Tr}_{kk'}^1 + 2\text{Tr}_{kk'}^2 + \text{Tr}_{kk'}^3}{4} \right) X_{kk'pt} + \\ & \sum_{j=1}^J \sum_{p=1}^P \sum_{t=1}^T \sum_{r=1}^t H_j \ln_{jptr} + \sum_{k=1}^K \sum_{p=1}^P \sum_{t=1}^T \sum_{e=r}^t H_k \ln_{kptre} \end{aligned} \quad (31)$$

$$\gamma \geq \left(\alpha \left(\frac{D_{hpt}^2 + D_{hpt}^3}{2} \right) + (1 - \alpha) \left(\frac{D_{hpt}^1 + D_{hpt}^2}{2} \right) \right) - \sum_{k=1}^K X_{khpt}, \quad \forall h, p, t \quad (32)$$

In the fuzzy planning model, the value of the uncertainty rate to establish the non-deterministic limit should be determined by considering the decision-making preferences. As can be seen, in relation (31), the objective function is not sensitive to the deviation from its expected value, which means that achieving stable solutions in the above model is not guaranteed. In such cases, high risk may be imposed on the decision-making in many real cases, especially in strategic decisions where the stability of the solution is critical to a large extent. Therefore, to address this inefficient situation, a robust non-deterministic planning approach is employed for the problem. This approach leverages the significant advantages of both robust planning and non-deterministic planning, which clearly distinguishes it from other approaches to uncertainty planning. In this research, uncertainty planning is applied based on the presented model, which is as follows:

$$\text{Min } Z_1 = E[Z_1] + \xi(Z_{1(\max)} - E[Z_1]) + \quad (33)$$

$$\eta \sum_{h=1}^H \sum_{p=1}^P \sum_{t=1}^T [D_{hpt}^3 - \alpha D_{hpt}^3 - (1 - \alpha) D_{hpt}^2]$$

$$\text{Min } Z_2 = \gamma \quad (34)$$

s. t.

$$E[Z_1] = \sum_{i=1}^J F_i Y_i + \sum_{j=1}^J F_j Y_j + \sum_{k=1}^K F_k Y_k + \quad (35)$$

$$\begin{aligned}
& \sum_{i=1}^I \sum_{j=1}^J \sum_{p=1}^P \sum_{t=1}^T \left(\frac{\text{Tr}_{ij}^1 + 2\text{Tr}_{ij}^2 + \text{Tr}_{ij}^3}{4} \right) X_{ijpt} + \\
& \sum_{j=1}^J \sum_{k=1}^K \sum_{p=1}^P \sum_{t=1}^T \left(\frac{\text{Tr}_{jk}^1 + 2\text{Tr}_{jk}^2 + \text{Tr}_{jk}^3}{4} \right) X_{jkpt} + \\
& \sum_{k=1}^K \sum_{h=1}^H \sum_{p=1}^P \sum_{t=1}^T \left(\frac{\text{Tr}_{kh}^1 + 2\text{Tr}_{kh}^2 + \text{Tr}_{kh}^3}{4} \right) X_{khpt} + \\
& \sum_{k=1}^K \sum_{k'=1}^K \sum_{p=1}^P \sum_{t=1}^T \left(\frac{\text{Tr}_{kk'}^1 + 2\text{Tr}_{kk'}^2 + \text{Tr}_{kk'}^3}{4} \right) X_{kk'pt} + \\
& \sum_{j=1}^J \sum_{p=1}^P \sum_{t=1}^T \sum_{r=1}^t H_j \text{In}_{jp\text{tr}} + \sum_{k=1}^K \sum_{p=1}^P \sum_{t=1}^T \sum_{e=r}^t \sum_{r=1}^t H_k \text{In}_{kp\text{tre}} \\
Z_{1(\text{max})} = & \sum_{i=1}^I F_i Y_i + \sum_{j=1}^J F_j Y_j + \sum_{k=1}^K F_k Y_k + \sum_{i=1}^I \sum_{j=1}^J \sum_{p=1}^P \sum_{t=1}^T \text{Tr}_{ij}^3 X_{ijpt} + \\
& \sum_{j=1}^J \sum_{k=1}^K \sum_{p=1}^P \sum_{t=1}^T \text{Tr}_{jk}^3 X_{jkpt} + \sum_{k=1}^K \sum_{h=1}^H \sum_{p=1}^P \sum_{t=1}^T \text{Tr}_{kh}^3 X_{khpt} + \sum_{j=1}^J \sum_{p=1}^P \sum_{t=1}^T \sum_{r=1}^t H_j \text{In}_{jp\text{tr}} + \\
& \sum_{k=1}^K \sum_{k'=1}^K \sum_{p=1}^P \sum_{t=1}^T \text{Tr}_{kk'}^3 X_{kk'pt} + \sum_{k=1}^K \sum_{p=1}^P \sum_{t=1}^T \sum_{e=r}^t \sum_{r=1}^t H_k \text{In}_{kp\text{tre}}
\end{aligned} \tag{36}$$

$$\gamma \geq \left(\alpha \left(\frac{D_{\text{hpt}}^2 + D_{\text{hpt}}^3}{2} \right) + (1 - \alpha) \left(\frac{D_{\text{hpt}}^1 + D_{\text{hpt}}^2}{2} \right) \right) - \sum_{k=1}^K X_{khpt}, \quad \forall h, p, t \tag{37}$$

$$\sum_{r=1}^t \text{In}_{jp\text{tr}} = \sum_{i=1}^I X_{ijpt} - \sum_{k=1}^K X_{jkpt}, \quad \forall j, p, t = 1 < v_p \tag{38}$$

$$\sum_{r=1}^t \text{In}_{jp\text{tr}} = \sum_{r=1}^{t-1} \text{In}_{jp\text{tr}} + \sum_{i=1}^I X_{ijpt} - \sum_{k=1}^K X_{jkpt}, \quad \forall j, p, 1 < t < v_p \tag{39}$$

$$\sum_{r=t+1-v_p}^t \text{In}_{jp\text{tr}} = \sum_{r=t+1-v_p}^{t-1} \text{In}_{jp\text{tr}} + \sum_{i=1}^I X_{ijpt} - \sum_{k=1}^K X_{jkpt}, \quad \forall j, p, t \geq v_p \tag{40}$$

$$X_{jkpt} = \sum_{r=1}^t U_{jkp\text{tr}}, \quad \forall j, k, p, t < v_p \tag{41}$$

$$X_{jkpt} = \sum_{r=t+1-v_p}^t U_{jkp\text{tr}}, \quad \forall j, k, p, t \geq v_p \tag{42}$$

$$\text{In}_{jp\text{tr}} = \sum_{i=1}^I X_{ijpt} - \sum_{k=1}^K U_{jkp\text{tr}}, \quad \forall j, p, r = t \tag{43}$$

$$In_{jp\text{tr}} = In_{jp\text{t}-1r} - \sum_{k=1}^K U_{jkp\text{tr}}, \quad \forall j, p, t - r < v_p \quad (44)$$

$$\sum_{e=r}^t \sum_{r=1}^t In_{kp\text{tre}} = \sum_{j=1}^J X_{jkp\text{t}} - \sum_{h=1}^H X_{khp\text{t}} + \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{k'kp\text{t}} - \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{kk'p\text{t}}, \quad \forall k, p, t = 1 < v_p \quad (45)$$

$$\sum_{e=r}^t \sum_{r=1}^t In_{kp\text{tre}} = \sum_{e=r}^{t-1} \sum_{r=1}^{t-1} In_{kp\text{t}-1re} + \sum_{j=1}^J X_{jkp\text{t}} - \sum_{h=1}^H X_{khp\text{t}} + \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{k'kp\text{t}} - \quad (46)$$

$$\sum_{\substack{k'=1 \\ k \neq k'}}^K X_{kk'p\text{t}}, \quad \forall k, p, 1 < t < v_p$$

$$\sum_{e=r}^{r+v_p-1} \sum_{r=t-v_p+1}^t In_{kp\text{tre}} = \sum_{e=r}^{t-1} \sum_{r=t-v_p+1}^{t-1} In_{kp\text{t}-1re} + \sum_{j=1}^J X_{jkp\text{t}} - \sum_{h=1}^H X_{khp\text{t}} + \quad (47)$$

$$\sum_{\substack{k'=1 \\ k \neq k'}}^K X_{k'kp\text{t}} - \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{kk'p\text{t}}, \quad \forall k, p, t \geq v_p$$

$$X_{khp\text{t}} = \sum_{e=r}^t \sum_{r=1}^t S_{khp\text{ret}}, \quad \forall k, h, p, t < v_p \quad (48)$$

$$X_{khp\text{t}} = \sum_{e=r}^{r+v_p-1} \sum_{r=t-v_p+1}^t S_{khp\text{ret}}, \quad \forall k, h, p, t \geq v_p \quad (49)$$

$$X_{k'kp\text{t}} = \sum_{e=r}^t \sum_{r=1}^t V_{k'kp\text{ret}}, \quad \forall k, k', p, t < v_p \quad (50)$$

$$X_{k'kp\text{t}} = \sum_{e=r}^{r+v_p-1} \sum_{r=t-v_p+1}^t V_{k'kp\text{ret}}, \quad \forall k, k', p, t \geq v_p \quad (51)$$

$$In_{kp\text{tre}} = \sum_{j=1}^J U_{jkp\text{tr}} - \sum_{h=1}^H S_{khp\text{ret}} + \sum_{\substack{k'=1 \\ k \neq k'}}^K V_{k'kp\text{ret}} - \sum_{\substack{k'=1 \\ k \neq k'}}^K V_{kk'p\text{ret}}, \quad \forall k, p, r, e = t \quad (52)$$

$$In_{kp\text{tre}} = In_{kp\text{t}-1re} - \sum_{h=1}^H S_{khp\text{ret}} - \sum_{\substack{k'=1 \\ k \neq k'}}^K V_{kk'p\text{ret}}, \quad \forall k, p, r, t - e < v_p \quad (53)$$

$$\sum_{j=1}^J X_{ijp\text{t}} \leq Cap_{ip} \cdot Y_i, \quad \forall i, p, t \quad (54)$$

$$\sum_{i=1}^I X_{ijp\text{t}} \leq Cap_{jp} \cdot Y_j, \quad \forall j, p, t \quad (55)$$

$$\sum_{j=1}^J X_{jkpt} + \sum_{\substack{k'=1 \\ k \neq k'}}^K X_{k'kpt} \leq \text{Cap}_{kp} \cdot Y_k, \quad \forall k, p, t \quad (56)$$

$$\sum_{r=1}^t \text{In}_{jptr} \geq \text{ss}_{jpt} \cdot Y_j, \quad \forall j, p, t \quad (57)$$

$$\sum_{e=r}^t \sum_{r=1}^t H_k \text{In}_{kptre} \geq \text{ss}_{kpt} \cdot Y_k, \quad \forall k, p, t \quad (58)$$

$$\text{In}_{jptr} = 0, \quad \forall j, p, t < r \quad (59)$$

$$\text{In}_{kptre} = 0, \quad \forall k, p, e, t < r \quad (60)$$

$$\text{In}_{kptre} = 0, \quad \forall k, p, r, e < r \quad (61)$$

$$X_{ijpt}, X_{jkpt}, X_{khpt}, X_{kk'pt}, U_{jkprt}, S_{khpret}, V_{kk'pret}, \text{In}_{jptr}, \text{In}_{kptre} \geq 0, \quad \forall i, j, k, k', h, p, t, e, r \quad (62)$$

$$Y_i, Y_j, Y_k \in \{0,1\}, \quad \forall i, j, k \quad (63)$$

In equation (33), the first term refers to the expected value of the first objective function using the average values of the uncertain parameters of the model. The second term refers to the penalty cost for deviation from the expected value of the first objective function (stability of optimality). The third sentence also shows the total cost of the penalty for deviation from the demand (non-deterministic parameter). Therefore, the parameter ξ is the weight coefficient of the objective function, and η is the penalty cost of not estimating the demand. The parameter α , as an uncertainty rate, shows the value of the levels of fuzzy numbers, which should be a number between 0.1 and 0.9

4. Solution Method

The model presented in this article encompasses various decisions, including location and allocation. Therefore, this model can be reduced to the facility location problem, which has been proven in the literature [59, 60]. These types of problems are among the NP-hard problems. As a result, the minimum degree of difficulty of the drug SC model in this research is the same as the difficulty of the facility location model. Hence, it can be concluded that the designed model is NP-hard and meta-heuristic algorithms should be used to solve it (Mirzavand Boroujeni & Moradi, [61]). In this article, the MOGWO algorithm is used to solve the problem.

4.1. MOGWO Algorithm

The gray wolf, *Canis Lupus*, belongs to the Canidae family. Gray wolves are predators at the top of the food pyramid, meaning they are at the top of the food chain. Gray wolves mostly prefer to live in groups. The average pack size is 5-12 wolves. The leaders consist of one male and one female, who are referred to as Alpha. Alpha is primarily responsible for making decisions about hunting, where to sleep, when to wake up, etc.

Alpha's decisions are communicated to the group; However, some democratic behavior has also been observed where an Alpha obeys the other wolves in the pack. In congregations, the entire herd acknowledges the Alpha by lying low. The Alpha wolf is also the dominant wolf because the group must follow her orders. Alpha wolves are only allowed to mate in packs. It is worth noting that the Alpha is not necessarily the strongest member of the herd, but the best member in terms of management in the herd. The second level in the Gray Wolves hierarchy is Beta. Betas are subordinate wolves who assist the Alpha in making decisions or other pack decisions. Beta wolf can be male or female, and he is the best replacement for the Alpha if he dies or gets old. Beta executes

Alpha's commands throughout the herd and gives feedback to Alpha. The Omega Wolf is the lowest rank in the Gray Wolf hierarchy. Omega wolf plays the role of victim. Usually, Omega Wolves must obey all high-level and dominant Wolves. They are the last wolves allowed to eat. If the wolf is not an Alpha or an Omega, it is called a Delta. Delta wolves must be subordinate to the Alpha and Beta. However, they dominate Omega.

In the mathematical modeling of the social hierarchy of wolves, (α) Alpha is considered the most appropriate solution. Subsequently, (β) Beta and (δ) Delta are the second and third suitable solutions. The rest of the candidate solutions are assumed to be Omega (X). To hunt, gray wolves must find and surround prey. Therefore, the following equations update the positions of the wolves around the prey.

$$\vec{D} = |\vec{C} \cdot \vec{X}_p(t) - \vec{X}(t)| \quad (64)$$

$$\vec{X}(t+1) = \vec{X}(t) - \vec{A} \cdot \vec{D} \quad (65)$$

In the above equation, $|\vec{C}|$ and \vec{A} are coefficient vectors. (\vec{X}_p) is the position vector of prey and \vec{X} is the position vector of gray wolves. It is a balancing act between siege and hunting. Therefore, the search radius must be optimized during the process. For this purpose, the equations related to the two coefficients used in the above relationships are as follows.

$$\vec{A} = 2\vec{a} \cdot \vec{r}_1 - \vec{a} \quad (66)$$

$$\vec{C} = 2\vec{r}_2 \quad (67)$$

The above equations enable gray wolves to update their position around the prey. As a result, the following equations are used for hunting.

$$\vec{D}_\alpha = |\vec{C}_1 \cdot \vec{X}_\alpha - \vec{X}|, \vec{D}_\beta = |\vec{C}_2 \cdot \vec{X}_\beta - \vec{X}|, \vec{D}_\delta = |\vec{C}_3 \cdot \vec{X}_\delta - \vec{X}| \quad (68)$$

$$\vec{X}_1 = \vec{X}_\alpha - \vec{A}_1 \cdot \vec{D}_\alpha, \vec{X}_2 = \vec{X}_\beta - \vec{A}_2 \cdot \vec{D}_\beta, \vec{X}_3 = \vec{X}_\delta - \vec{A}_3 \cdot \vec{D}_\delta \quad (69)$$

$$\vec{X}(t+1) = \frac{\vec{X}_1 + \vec{X}_2 + \vec{X}_3}{3} \quad (70)$$

4.2. Initial Answer

The initial solution stated is the well-known priority-based encoding introduced by Ghahremani *et al.*, [62]. In this encryption, the SC network is divided into its constituent levels, and each level is considered according to the capacity and demand in the chromosome design. Figure 3 shows an example of a two-level SC network with three sources and four depots. In this form, the location is done on the resources, and the resources must estimate the demands of the depot.

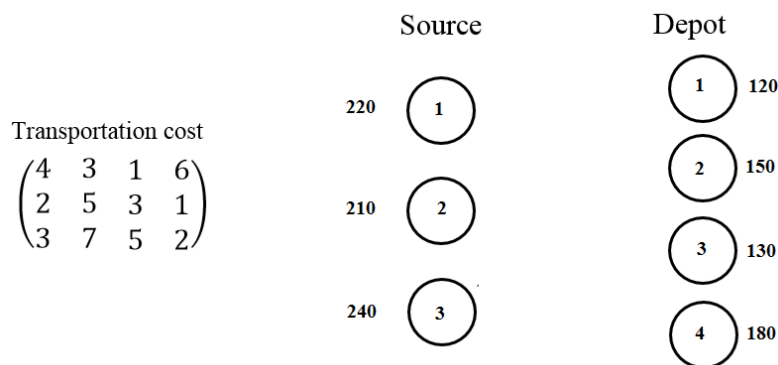


Fig. 3. An example of a two-level SC network

4.3. Indicators of Comparison of Practical Answers

The multi-objectiveness of mathematical models leads to the creation of different efficient solutions by different solution methods, which makes it difficult to compare the efficient solutions and make decisions about the performance of the solution method. Therefore, the following indices are used to compare the efficient solutions created by different solution methods.

Calculation time (CPU-Time): The solution method that has less calculation time will be more favorable.

The number of solutions in Pareto (NPF) shows the number of non-defeated solutions in the Pareto set obtained for each problem, and the higher the number of these points, the more effective the solution method.

Maximum expansion (MSI): This measure shows how much of the solutions of a Pareto set in the distributed solution space is calculated from equation (71). The larger value of this criterion indicates the appropriate variety of solutions of the Pareto set.

$$MSI = \sqrt{\sum_{m=1}^M (\max_{i=1:|Q|} f_m^i - \max_{i=1:|Q|} f_m^i)^2} \quad (71)$$

Metric distance (SM): It indicates the degree to which the answers are uniformly placed together, which is calculated from equation (72).

$$SM = \sqrt{\frac{1}{|Q|} \sum_{i=1}^{|Q|} \left(d_i - \sum_{i=1}^{|Q|} \frac{\min_{k \in Q \cap k \neq i} \sum_{m=1}^M |f_m^i - f_m^k|}{|Q|} \right)^2} \quad (72)$$

In the above relation, $|Q|$ represents the size of the Pareto archive. The solution method that has a lower amount of this criterion will be more favorable.

5. Analysis of the Results

The model presented in the previous section is a drug SC model based on the IoT and BD, where primary information is collected through IoT tools and recorded in the database. The framework presented in this article utilizes the MOGWO algorithm and the epsilon constraint method to optimize two objective functions: minimizing total costs and minimizing the maximum unmet demand, based on data from the country's pharmaceutical industry. Based on this, by collecting data from hospitals and analyzing the drugs Rebif44 and Rebif22, which are used in the treatment of MS, the real demand for this drug has been obtained as described in Table 1. The shelf life of this medicine is 6 months, and the data were collected in 8 periods of 6 months.

Table 1

The actual drug demand of Rebif44 and Rebif22 drugs

Province Period	Rebif 22								Rebif 44							
	1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8
East Azerbaijan	238	212	208	200	210	172	222	206	222	210	130	148	122	124	196	210
West Azerbaijan	68	92	99	61	104	62	96	73	103	62	102	106	110	90	112	107
Ardabil	66	86	91	68	106	16	108	69	119	67	103	68	113	70	65	107
Isfahan	246	231	228	303	282	276	309	204	342	234	336	195	324	210	276	291
Alborz	78	117	69	91	62	83	77	111	88	107	83	109	89	73	95	107
Ilam	66	76	119	120	69	100	115	118	19	119	115	61	72	107	81	65
Bushehr	102	103	83	107	95	118	115	67	6	108	61	63	120	109	112	69

Table 1

Continued

Province Period	Rebif 22								Rebif 44							
	1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8
Tehran	310	455	330	510	405	550	430	375	580	500	410	305	590	320	455	310
Chaharmahal and Bakhtiari	63	74	117	78	67	109	79	118	73	61	97	62	63	75	100	118
South Khorasan	87	74	78	104	101	90	71	75	96	100	113	17	70	67	9	105
Razavi Khorasan	472	452	320	436	432	312	296	364	316	468	440	38	424	252	380	356
North Khorasan	66	104	114	109	107	107	99	81	112	70	103	70	115	72	112	86
Khuzestan	120	93	62	75	78	89	85	63	106	108	96	109	80	74	75	105
Zanjan	75	103	99	114	92	65	60	105	94	85	111	67	117	70	92	83
Semnan	88	91	68	12	70	118	120	112	85	70	68	77	96	84	105	71
Sistan and Baluchestan	77	16	120	107	103	6	89	68	72	72	81	60	85	97	74	64
Fars	99	102	76	99	102	78	99	99	68	80	117	70	117	120	110	120
Qazvin	68	105	112	78	64	108	110	102	69	115	93	101	92	117	65	97
Qom	94	79	118	82	68	60	116	95	76	66	75	98	66	104	94	107
Kurdistan	81	73	83	88	104	120	20	66	68	103	82	106	96	97	101	76
Kerman	76	98	90	66	98	92	94	72	95	107	97	118	114	74	64	93
Kermanshah	93	93	76	116	102	61	119	113	63	79	100	110	82	77	86	117
kohgiluyeh and Boyer- Ahmad	69	65	101	66	115	95	98	97	81	80	120	72	107	81	95	69
Golestan	156	136	232	230	138	194	120	13	16	240	210	172	224	142	236	176
Gilan	71	62	89	91	3	99	91	119	70	109	72	103	62	113	104	80
LoRESTAN	117	14	73	105	96	70	100	92	95	95	89	82	61	86	61	94
Mazandaran	120	6	68	71	96	63	93	104	105	95	118	114	91	118	70	79
Markazi	76	93	103	68	106	109	71	72	81	113	64	96	105	92	96	110
Hormozgan	10	120	116	101	77	95	107	82	80	80	70	108	98	104	111	120
Hamedan	102	96	86	98	104	120	82	107	67	82	87	117	79	67	113	61
Yazd	104	73	109	77	116	67	101	92	71	86	112	65	75	100	90	72

Additionally, the definite and non-deterministic parameters of the model have been determined based on the opinions of the country's pharmaceutical industry experts, as presented in Table 2.

Table 2

Value of deterministic and non-deterministic parameters of the problem

Parameter	Parameter range
F_i, F_j, F_k	$\sim U(150000, 200000)\$$
H_j, H_k	$\sim U(2, 5)\$$
$\overline{Tr}_{ij}, \overline{Tr}_{jk}, \overline{Tr}_{kk'}, \overline{Tr}_{kh}$	Optimistic: $\sim U(5, 10)\$$ Likely: $\sim U(10, 15)\$$ Pessimistic: $\sim U(15, 20)\$$
\tilde{D}_{hpt}	Optimistic: $0.95 * D_{hpt}$ Likely: D_{hpt} Pessimistic: $1.05 * 0.95 * D_{hpt}$
v_p	6 mounth
$Cap_{ip}, Cap_{jp}, Cap_{kp}$	$\sim U(500, 1500)$
SS_{jpt}, SS_{kpt}	$\sim U(20, 50)$

After analyzing the extensive data on the country's PSC, a set of practical solutions is presented in Table 3. These results are derived from the MOGWO algorithm as a meta-heuristic method and

the epsilon constraint method as an exact method. Also, the Pareto front resulting from solving the mathematical model is obtained in the form of (5).

Table 3

Set of practical solutions to the problem

Solution	MOGWO		Epsilon Constraint	
	Total Cost (1000 \$)	Max γ	Total Cost (1000 \$)	Max γ
1	1303212.72	78	1301004.25	76
2	1313012.22	75	1338565.34	66
3	1323940.05	72	1360836.68	63
4	1331755.14	69	1381979.19	60
5	1366206.29	62	1408254.02	56
6	1392788.73	58	1434352.94	52
7	1408514.98	55	1485472.42	47
8	1433304.81	53	-	-
9	1466833.13	50	-	-
10	1474332.49	49	-	-
11	1498842.94	47	-	-

According to the results of Table 3, it can be seen that by reducing the maximum number of unfulfilled Rebif 22 and Rebif 44 drugs, the costs of the entire drug SC network in Iran have increased. Also, 11 different efficient solutions from the MOGWO method and seven efficient solutions from the epsilon constraint method have emerged for this problem, in which each of the efficient solutions has an advantage over the other. Based on the results of Table 3, the obtained Pareto front will be in accordance with Figure 6.

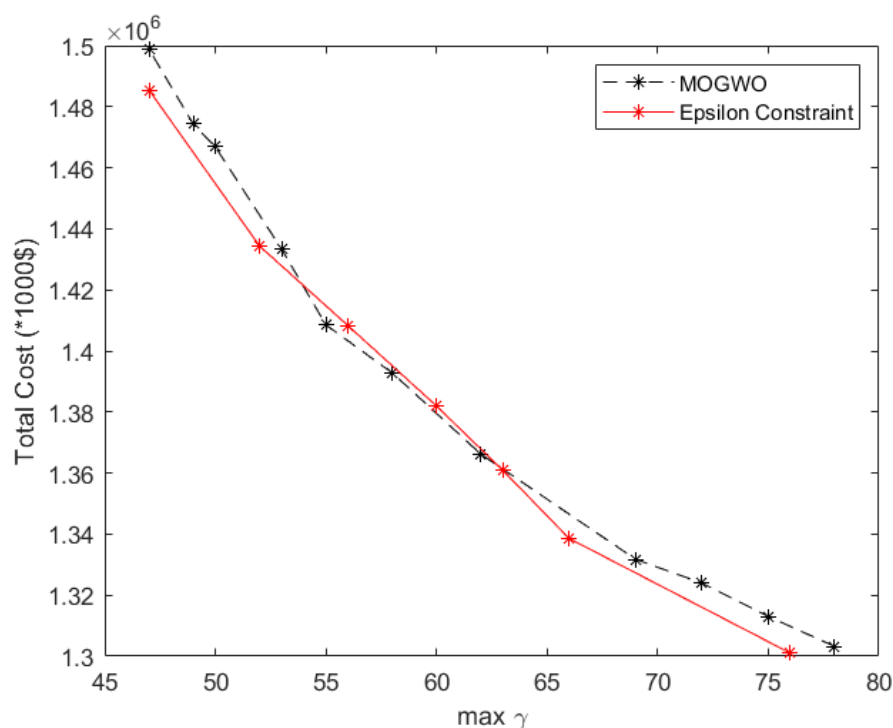


Fig. 6. Pareto front obtained from solving the case study

The results of Figure 6 show that by decreasing the value of the second objective function (paying more attention to the social aspects of the problem), the value of the first objective function

(economic aspects of the problem) increases. Since two different methods have been used to solve the problem, comparison indices have been used to compare the efficient solutions. Table 4 shows the comparison indexes of effective solutions between two different solution methods.

Table 4

Indicators of comparison of practical solutions in solving the problem of Iran's drug SC

Solution Approach	NPF	MSI	SM	CPU-Time
MOGWO	11	195630.22	0.427	68.49
Epsilon Constraint	7	184468.17	0.216	1342.15

The results of Table 4 show that the MOGWO algorithm has obtained 11 different efficient solutions in 68.49 seconds. Also, the value of the MSI index in this method is higher than the limit epsilon method. Therefore, by examining various indicators, it can be seen that the use of this analysis tool is more efficient than the detailed methods for designing the drug SC network, and the output of the problem is presented based on this solution tool.

Since 11 different efficient solutions have been obtained from solving the drug SC problem with an emphasis on IoT and BD, only the results of the first efficient solution have been shown to examine the outputs of the problem. Therefore, in Figure 7, raw material suppliers, production centers, and potential warehouses selected from the BD analysis are shown.

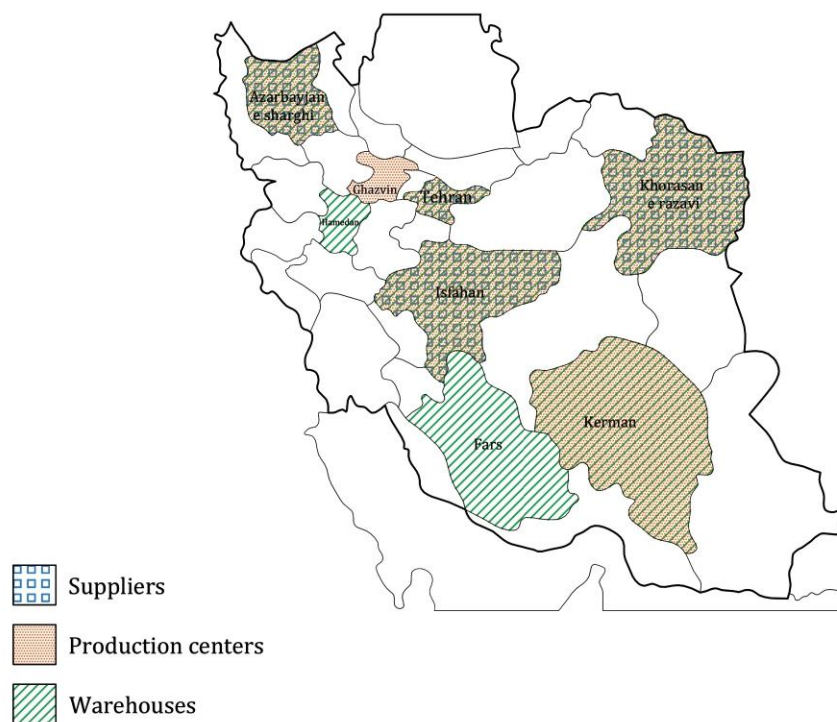


Fig. 7. Raw material suppliers, production centers, and potential warehouses selected from BD analysis

Additionally, Figure 8 illustrates the supply of Rebif 22-44 drugs by the warehouses of each province in the country. In this form, each of the provinces can cover the demand of the stated provinces.



Fig. 8. Provinces covered by each central warehouse

After examining the most optimal mode of supplier selection as well as the allocation of the flow of goods transfer between different levels of the SC network, the impact of rapid changes in the problem parameters on the objective functions has been investigated. Since the collection of information is through IoT tools such as RFID, sensors, etc., in case of a change in the status of any of the parameters, the type of allocation and the way of transferring drugs between the origin and the destination may be changed, and this leads to an increase or a reduction in total costs. In the following, assuming a change in the duration of the drug's perishability, the total cost of the SC is illustrated. Forasmuch as the MOGWO algorithm has the best performance in terms of achieving the objective function in a short period of time, this tool has been used for sensitivity analysis.

In Table 5, the changes in the value of the objective function have been examined for the changes in the uncertainty rate in the drug SC network. In this analysis, by increasing/decreasing the uncertainty rate, the changes in the value of the objective functions of the problem are shown.

Table 5

Changes in the value of the objective function of the problem for changes in the uncertainty rate

α	Total Cost (1000 \$)	Max γ
0.1	1252318.67	70
0.2	1268417.62	73
0.3	1276744.45	75
0.4	1296387.48	77
0.5	1303212.72	78
0.6	1312498.67	79
0.7	1322498.24	80
0.8	1349846.49	82
0.9	1359865.02	84

According to the results of Table 5, it can be seen that with the increase of the uncertainty rate and based on the information collected by the sensors and data processing tools, it is observed that the amount of Rebif22-44 drug demand has increased, and this has led to an increase in the shortage in the SC network. There has also been an increase in the costs associated with meeting the demand of hospitals for MS drugs. This indicates that, in the most pessimistic scenario, the costs of the drug SC network will be as high as the maximum amount of demand shortage in Iran. Figure 9 shows the changes in the values of the objective functions of the problem at different rates of uncertainty.

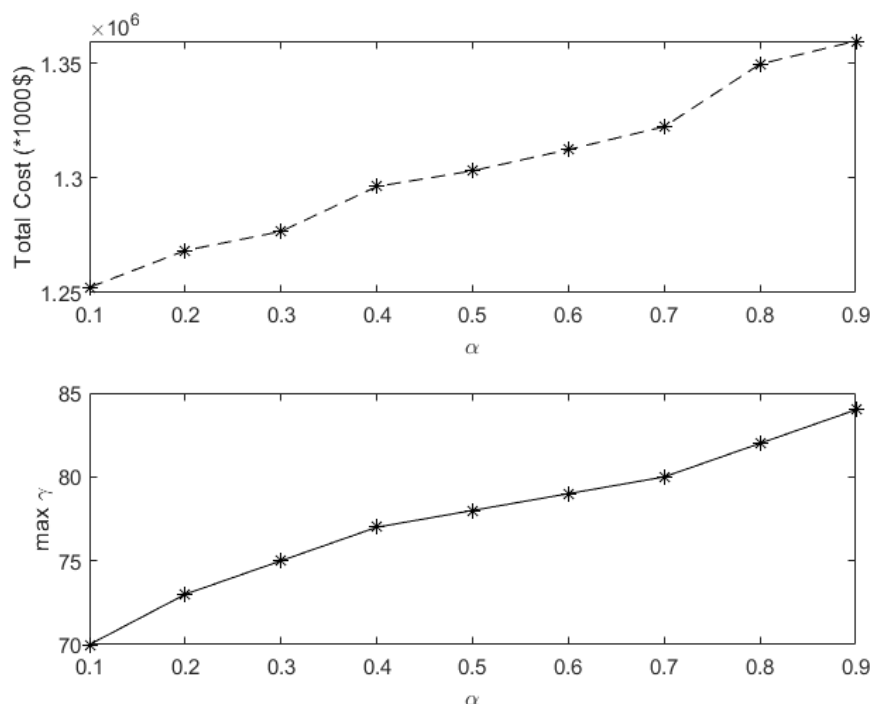


Fig. 9. The trend of changes in the value of the objective function of the problem for changes in the uncertainty rate

Additionally, with the aid of IoT tools, it is possible to quickly and efficiently check the production status and identify any disruptions in the system. Therefore, if there is a breakdown of the drug production devices, as well as a reduction in the amount of production capacity in the event of a disruption, the costs of the entire SC can be estimated based on the presented mathematical model. Table 6 examines the cost changes of the whole SC against the reduction of production capacity.

Table 6

Changes in the value of the objective function of the problem for changes in the production capacity

Production Capacity Usage Rate	Total Cost (1000 \$)	Max γ
100 %	1303212.72	78
90 %	1303212.72	78
80 %	1326475.28	79
70 %	1386478.22	80
60 %	1423645.64	85
50 %	1467745.14	91

Based on the analysis, it can be seen that with the reduction in production capacity, due to changes in the type of drug allocation and transfer, as well as the use of other centers for drug production, the costs of the entire SC network have increased. The shortage of drugs in the country has also increased. If the production capacity of all units is reduced by 50%, the total costs will be 1467745.14 thousand dollars. Figure 10 shows the trend of changes in the cost of the entire SC for changes in production capacity.

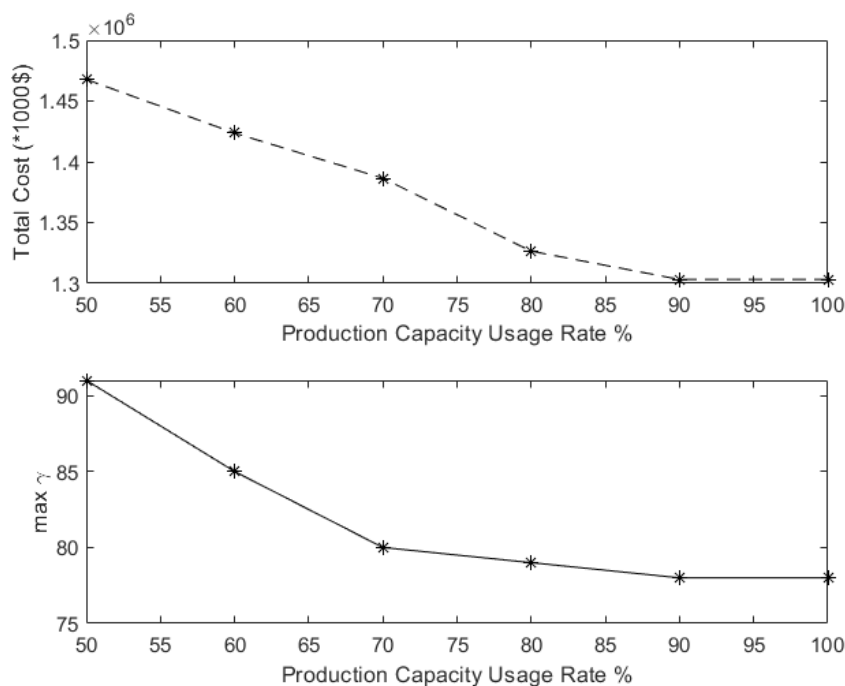


Fig. 10. The trend of changes in the value of the objective function of the problem for changes in the production capacity

6. Conclusion and Future Suggestions

This article presents an agile framework for the drug SC, with a focus on the utilization of IoT and BD analysis. The primary purpose of providing such a framework is to provide structured data on the country's pharmaceutical industry, based on IoT tools such as sensors and RFID. Additionally, analyzing large datasets to optimize the country's drug SC was another key goal of the article. For this, a 4-level drug SC consisting of suppliers, production centers, warehouses, and hospitals was designed. In this model, two objective functions of minimizing the costs of the entire SC network and minimizing the maximum unfulfilled demand are considered.

After collecting vast amounts of data through IoT tools, the epsilon limit method and MOGWO algorithm were employed to optimize the model and analyze the data using the mathematical model. As a result of this, it was observed that 11 efficient solutions were obtained from the MOGWO algorithm, and seven efficient solutions were obtained from the epsilon limit method for the preparation of Rebif 22-44 medicine in Iran. By comparing the two approaches, it was observed that the MOGWO algorithm yields more efficient solutions in a significantly shorter time. The result of this was the selection of 4 provinces of Tehran, Isfahan, East Azerbaijan, and Razavi Khorasan as drug suppliers. On the other hand, the provinces covered by each selected warehouse were specified. The results of the sensitivity analysis also showed that as the uncertainty rate in the network increased, the actual demand for the medicine also increased, leading to a corresponding rise in shortages.

Compared with a counterfactual non-IoT baseline (i.e., delayed/low-granularity data), the IoT-enabled case achieved a markedly better service level at a quantifiable cost: lowering the maximum unmet demand from 78 to 47 units required increasing total network cost from 1,303,212.72 to 1,498,842.94 (USD), demonstrating that IoT-driven visibility and big-data analytics improve shortage outcomes while tracing the exact cost–equity trade-off.

For future research, it is suggested that new meta-heuristic algorithms be employed to enhance problem-solving and uncertainty control within the model. Also, the examination of other drugs is indicated in Iran. Beyond the above, future research should also: (i) examine IoT–Blockchain architectures for end-to-end authenticity and cold-chain compliance; (ii) integrate Edge-AI/Digital Twins for real-time control and predictive maintenance; (iii) employ privacy-preserving/federated learning for multi-hospital demand forecasting; (iv) extend robust/stochastic modeling to ripple-effect disruptions with richer scenario design; and (v) benchmark additional multi-objective solvers (e.g., NSGA-II/III, MOEA/D, AUGMECON2) and learning-augmented heuristics against the proposed MOGWO/ ϵ -constraint pipeline.

Author Contributions

Conceptualization, A.R. and S.E.N.; methodology, A.R. and S.E.N. and M.Kh. ; software, A.R. , S.E.N and M.Kh.; validation, S.E.N., M.Kh. and H.K.; formal analysis, A.R. , S.E.N. and M.Kh. ; investigation, A.R., S.E.N and M.Kh; resources, A.R. , S.E.N and M.Kh; data curation, A.R.; writing—original draft preparation, A.R. and S.E.N.; writing—review and editing, A.R. , S.E.N , M.Kh. and H.K.; visualization, A.R. and S.E.N.; supervision, S.E.N. and M.Kh.; project administration, S.E.N.; funding acquisition, A.R and S.E.N. All authors have read and agreed to the published version of the manuscript.

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All data used in this study are included in this article.

Conflicts of 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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