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Research Article

A Mathematical Optimization Model for the Pharmaceutical Waste Location-Routing Problem Using Genetic Algorithm and Particle Swarm Optimization

Sina Aghakhani[1], **Parmida Pourmand**[2] **and Mobin Zarreh**[2]

[1]*Department of Industrial and Manufacturing Systems Engineering, Iowa State University, Ames, IA, USA*
[2]*School of Industrial Engineering, Iran University of Science and Technology, Tehran, Iran*

Correspondence should be addressed to Parmida Pourmand; p6industrial@gmail.com

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Pharmaceutical waste management is a significant concern that poses risks to human and environmental health. The ineffective management of expired and unused medications can harm individuals and communities. This study proposes a novel approach to address the issue of pharmaceutical waste management by developing a location-routing problem (LRP) model using mixed-integer linear programing (MILP) to optimize the collection and disposal of pharmaceutical waste. The proposed model aims to minimize transportation costs, construction of collection centers, disposal costs, and carbon dioxide emissions, making it a cost-effective and environmentally sustainable approach to managing pharmaceutical waste. Initially, the feasibility, validity, and efficiency of the proposed model are examined by solving the problem in the GAMS software using CPLEX solver for small-scale problems. Sensitivity analyses are conducted to ensure the accuracy, reliability, robustness, and usefulness of the mathematical model for decision-making. In view of the inherent computational complexity of the proposed model, which is classified as nondeterministic polynomial time-hard and poses considerable difficulties when exact solutions are sought for large-scale problems, the present study resorts to two metaheuristic algorithms, specifically particle swarm optimization (PSO) and genetic algorithm (GA), as a means minimizing the computational burden. The results indicate that GA outperforms PSO in terms of objective function and solution time, with an average improvement of approximately 1% and 20%, respectively. The proposed model and algorithms provide a comprehensive approach to addressing the critical issue of pharmaceutical waste management, benefiting the healthcare industry, and society as a whole.

1. Introduction

In recent years, waste production has increased across the globe as a result of urbanization, population growth, and economic development. Due to this, it is critical to consider the environmental effects of solid waste. A total of 33% of the world's 2.01 billion tons of solid waste generated annually are uncollected, and that number is likely to increase to 3.40 billion tons by 2050 [1]. Consequently, solid waste management (SWM) is essential for preventing these challenges, which entails the collection, transportation, tracking, processing, disposal, or recycling of solid wastes [2]. Based on their source, solid wastes can be classified as municipal, hazardous, radioactive, or medical. Nevertheless, medical waste plays an extremely significant role in SWM throughout the world, as was demonstrated during the coronavirus pandemic. Among the most critical types of waste are medical wastes. Additionally, its management requires considerable attention due to its complexity. It is therefore imperative that medical waste is handled and disposed of properly, as it can be hazardous and toxic, posing a risk to the environment and the public good [3]. There has been a substantial increase in pharmaceutical waste over the past century due to increased patient numbers, prescriptions, consumption, and overproduction of medication, which constitutes the majority of medical waste. Therefore, pharmaceutical waste has ecological, financial, and ethical consequences that should be examined from several perspectives [4]. To consider the supply chain's environmental aspects, reverse logistics (RL) can be an effective solution. The reduction of carbon footprint is one of the benefits of using RL. In most cases, RL systems result in additional profits for companies in the long run [5]. Thus, the RL network for the pharmaceutical supply chain (PSC) provides significant benefits to society. A similar approach is taken by the circular economy (CE) within the PSC, which works to reduce waste, maximize the value of medicines, and ensure a sustainable supply chain [6, 7]. Medical waste management issues can be divided into three primary categories. Identifying the most efficient routes in each area is the first category. In the second category, it is necessary to evaluate where different facilities (such as recycling companies or separate waste disposal centers) should be located within the waste supply chain. As a result of combining the two categories previously mentioned, a third category is formed, known as location routing problems (LRPs). It deals with the routing and location of various SWM supply chain components [8].

In contrast, the LRP, which combines the facility location problem (FLP) and the vehicle routing problem (VRP), has been an essential tool in logistics since Maranzana [9] noted the need to determine the locations of facilities and delivery routes simultaneously. Furthermore, the CE is a holistic theory that promotes resource management and preservation through recycling and reuse [6]. Along with the previous definition above, RL is generally defined as the movement of materials and products in the opposite direction of the main flow. Thus, it has become significant to integrate CE and RL into the supply chain to foster environmental and economic growth [10]. It is given that the principal core of the CE is 3R, which is reduction, reuse, and recycling, it provides practical guidelines for reducing waste and encouraging recycling. Moreover, the main focus of RL is on return management, and it can be said that RL has a strong connection with CE regarding technical aspects [11]. As a result, CE and RL, along with LRP, are the best tools for engaging with waste management.

Healthcare plays a crucial role in life. Assessing the development level of a country is also a crucial factor. In contrast, healthcare is a significant source of pollution, but recycling such materials requires large budgets and unique techniques, and the global economy has been strained by rising healthcare costs in recent years. As a consequence, regulatory agencies identify drug-tracking collaboration and sharing as the most critical issues in healthcare [12]. However, despite various waste management studies, few have reported pharmaceutical waste management. While most studies on medical waste management have only focused on the management aspect, studies on analytical models, or quantity techniques are rare. Moreover, in the articles related to waste in the literature, the subject of waste is mainly discussed in a general way. Still, the field of medicine and its waste, due to the mentioned importance and different characteristics compared with the rest of the waste, requires a more focused investigation and involves its significance and characteristics. Moreover, in the waste collection field, separating expired drugs and drugs with an expiration date of less than 1 year to be sent to developing and deprived areas with less or no cost has rarely been addressed.

This study presents a multilevel supply chain model for efficient pharmaceutical waste management. The proposed model addresses the hazardous medical waste first and subsequently redirects the reusable medicines back into the supply chain. This approach can benefit countries with lower levels of welfare, by providing them access to these reusable medicines. Additionally, the model aims to minimize cost while taking into consideration the emission of carbon dioxide as a cost. Thus, the model not only reduces financial expenses but also mitigates the environmental impact. An initial evaluation of the model was conducted using GAMS at a small scale. Subsequently, the model was solved at a large scale through the application of two different metaheuristic algorithms; GA and PSO. The proposed model is a novel approach to address the issue of pharmaceutical waste management, with the potential to improve the efficiency of the healthcare supply chain and contribute to the establishment of a green supply chain.

The structure of this research article is organized as follows: Section 2 provides a summary of the related literature, specifically focusing on LRP, in relation to the case of pharmaceutical supply chain and waste management; Section 3 describes the problem and introduces a mathematical model for LRP; in Section 4, the solution approach for the proposed model is presented; Section 5 outlines the process of solving the proposed model on a small scale, to assess the sensitivity of the mathematical model to its modeling assumptions; Section 6 employs sensitivity analysis; in Section 7 the proposed model is solved on a medium and large scale in Section 7; managerial insights are presented in Section 8; finally, Section 9 concludes the research by summarizing the key findings and their implications for future research in this area.

2. Literature Review

In the literature, some scholars investigated medical and pharmaceutical waste recycling networks as supply chain network design and construction problems. The supply chain management helps companies to reduce operating costs, speed up processes, and ultimately increase customer satisfaction [13]. A number of these studies are presented. Lotfi et al. [14] presented the medical waste chain network design, which includes the landfill, waste purchase contractor (WPC), waste segregation (WS), and health center. They suggested finding WS, recovering them, and sending them to the WPC to reduce waste. Consequently, a novel two-stage robust stochastic programing method is proposed that considers sustainability and resilience. Ahmadi et al. [15] presented a mathematical model aimed at minimizing the costs of the entire chain, including fixed construction costs, transportation costs, and inventory holding costs, and minimizing the maximum unanswered demand. Besides, Kargar et al. [7] developed a linear programing model under uncertainty to design a medical waste reverse supply chain. The proposed multiitem and multiperiod model with three objective functions, minimizing the total cost, the best treatment technology, and the entire medical waste stored: a robust possibilistic programing approach and a fuzzy goal programing method were employed in modeling. From the standpoint of the producers of medical materials, Shi [16] addressed the design of the RL network for medical waste. In order to operate the RL network with the lowest possible operational costs, a mixed integer programing (MIP) model is built, and Lingo 8.0 to find the best solution is used. In the context of medical waste management, Sara and Btissam [17] presented the green RL network, and a model with multiple goals and products was created to reduce the network's adverse effects on the environment and minimize its reverse costs. Further, Taleizadeh et al. [18] examined the impact of uncertainty using robust optimization and made an effort to optimize reverse supply chain (RSC) members' profits to increase the returns of leftover medications and improve sustainability for a RSC in the pharmaceutical industry. Mei et al. [19] addressed the issue of locating facilities in a RL network. They proposed a multiperiod medical waste emergency RL network model to achieve this, with the objectives of minimizing costs, minimizing risk to safety, and maximizing response time for the disposal of medical waste.

In general, in order to reduce logistics costs or protect the environment from pollution such as CO_2 emissions, there are two approaches in the literature: in the first approach, special transport vehicles that produce low pollution, such as drones, are used. The amount of CO_2 emitted by these vehicles and logistics costs could be optimized by planning and modeling logistics networks [20, 21]. The second approach is to reduce logistics costs and environmental pollution by providing structures and methods for creating a distribution and collection logistics network. A good example of the second approach is the construction of collection or distribution centers or considering hierarchical hubs to reduce the number of vehicles and use vehicles with greater capacity, which leads to the reduction of logistics costs and environmental pollution [22].

To save the environment from the pollution brought on by greenhouse gas emissions, it is crucial to plan transportation routes and place facilities in the most advantageous locations possible for medical waste management. Hence, some of the papers that contributed to the VRP, FLP, and LRP applications focused on medical waste management are available in the following. In this work, Tirkolaee et al. [23] looked into a time-windowed sustainable multitrip LRP for managing medical waste. Adarang et al. [24] addressed an LRP under uncertainty for providing emergency medical services during disasters. Osaba et al. [25] aimed to design an algorithm that plans distribution and collection routes in such a way as to minimize the operating costs of the distribution company. Gao et al. [26] looked at a network of urban medical waste recycling to solve an integrated optimization problem. It merged the collecting issue for medical waste from clinics to the associated hospital with the vehicle routing issue for medical facilities with various requirements. They suggested a compact mixed-integer linear programing (MILP) model address this issue, considering the distinct collecting approach and time windows. To create a weekly inventory routing schedule to deliver medical waste to rehab centers, Taslimi et al. [27] looked into a periodic load-dependent capacitated VRP experienced by healthcare facilities and medical waste collecting businesses. The occupational risk associated with temporarily storing hazardous wastes at health centers is considered in addition to reducing transportation risk. The collection of medical waste in Northern Jordan was the subject of a stochastic model created by Alshraideh and Qdais [28]. To cut down on the overall trip distance, which lowers transportation costs and emissions, a route scheduling model was presented. A MILP model utilizing fixed routing optimization with static data and variable routing optimization with real-time data was developed to improve collection efficiency, save collection costs, and reduce emissions [2]. In the TRB1 region of Turkey, a geographic information system solution method is suggested by Mete and Serin [29] as a means of presenting a solution for the medical waste routing problem. Since a complete internal collection is crucial to reducing the risk to patients, hospital employees, visitors, and the surrounding environment, Hajar et al. [30] highlighted onsite healthcare waste collection. Tirkolaee and Aydın [31] created a biobjective MILP model, which is essentially a capacitated VRP, to address the issue of transportation planning and outsourcing of MWM services during pandemics and from a sustainability standpoint.

Globally, the unprecedented COVID-19 outbreak reinforced the critical importance of rapid development vs. survival for pharmaceutical companies and had a significant impact on the medical supply chain as well [32, 33]. During the COVID-19 outbreak, Govindan et al. [34] created a biobjective MILP model for managing medical waste to reduce the overall costs and dangers of the population's exposure to pollution. To handle both infectious and noninfectious medical waste, they also took into account several realistic hypotheses for the first time, including the LRP, the time window-based green VRP, the scheduling of vehicles, the failure of those vehicles, split deliveries, population risk, and load-dependent fuel consumption [35] proposed a novel multiobjective multiperiod MIP for RL network design, which aimed at determining the most effective temporary facility locations and transportation plans for handling the rapidly growing medical waste. To evaluate the influence of the coronavirus pandemic on the healthcare and noncold pharmaceutical care distribution supply chain, Abdolazimi et al. [36] developed a multiobjective model to minimize the total costs, environmental impacts, lead time, and the probability of a healthcare provider being infected by a sick person. Another research Goodarzian et al. [37] considered the distribution of medicines related to COVID-19 patients and modeled a multiobjective, multilevel, multiproduct, and multiperiod problem for a sustainable medical supply chain network being designed. In the study of Eren and Tuzkaya [38], a model for the safest and shortest route for the transportation of medical waste vehicles inside the city of Istanbul is provided. Scores used in this research came from Eren and Tuzkaya [39]. They were employed in a traveling salesman issue with multiple objectives to derive two objective functions based on safety scores and total travel distance. Table 1, summarizes the previous studies done regarding mathematical models in healthcare waste management.

While there are some existing papers that focus on PSC management, our paper focuses specifically on the challenges

Table 1: Summerized literature review.

Reference	Objective functions		Cost minimization				Problem type				Problem scale		Solution methodology
	Single	Multiple	Transportation	Collection centers	Disposal	Carbon dioxide emissions	Vehicle routing	Facility location	Location routing	Inventory routing	Small	Large	
[40]		✓	✓							✓			TH + hybridized possibilistic method
[41]		✓						✓					Fuzzy AHP + goal programing
[42]		✓						✓					Fuzzy AHP + fuzzy TOPSIS
[43]	✓		✓				✓				✓		Multistart iterated local search
[44]	✓		✓					✓					Artificial bee colony + clustering algorithms
[27]	✓		✓				✓			✓	✓	✓	Decomposition based heuristic
[23]		✓	✓		✓		✓	✓	✓		✓		Fuzzy chance-constrained programing
[7]		✓	✓	✓				✓			✓		Fuzzy goal programing
[45]		✓	✓			✓					✓		TH + Me
[34]		✓	✓	✓			✓				✓		IMCGP + GAM
[46]		✓	✓		✓							✓	LP-metrics + heuristic algorithm
[47]		✓	✓					✓			✓		Improved goal programing + Lp-metric
[48]	✓		✓							✓		✓	BOALNS
[49]		✓	✓				✓	✓	✓		✓	✓	(B and P) algorithm + μ-constraint
This study	✓		✓	✓	✓	✓	✓	✓	✓		✓	✓	Branch and bound algorithm for small-scale, GA + PSO

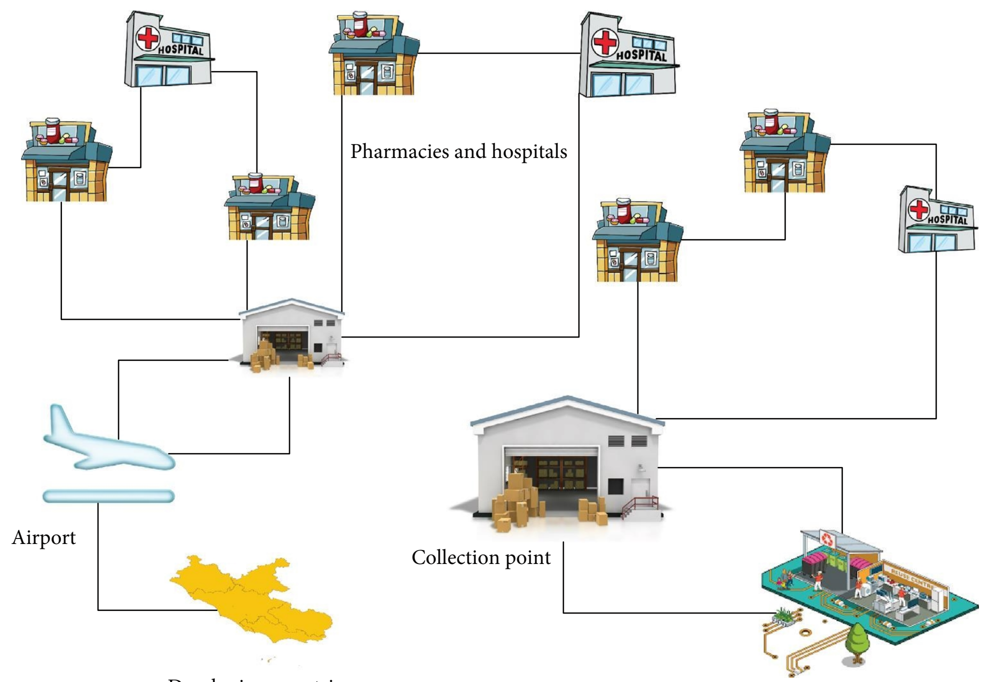

Figure 1: The designed supply chain.

of pharmaceutical waste management, while taking environmental considerations into account. Our article provides a comprehensive approach to managing pharmaceutical waste, taking into consideration various factors and proposing adaptable solutions suitable for different contexts. Furthermore, our research extends beyond small-scale problem solving, as we employ two distinct metaheuristic algorithms to solve our model at a larger scale. This allows us to provide insights into the effectiveness of our proposed model under a range of conditions, which has not been explored in previous literature. By filling this research gap, we hope to provide valuable contributions to the field of PSC management and waste reduction.

3. Problem Definition

This study considers a multiechelon supply chain, including distribution centers, customer points containing pharmacies and hospitals, collection centers, disposal centers, recycling centers, and airports. In this regard, pharmaceutical waste will be collected by vehicles and will be carried to the collection points that separate them. Medicines that expire in 1 year [50] are considered expired medicines and transferred to recycling and disposal centers to treat properly, which reduces the hazard risk of pharmaceutical waste. The unused medicines of patients with expiration dates of more than 1 year are sent to developing countries through airports so that they can use the medicines without paying any money; this will help those countries to increase the level of their societies' health. In this model, in addition to collecting pharmaceutical waste, the amount of carbon dioxide produced by vehicles will be reduced, that have an environmental aspect.

Furthermore, strategic determinations are undertaken regarding the optimal locations and number of collection centers. In other words, potential locations are carefully evaluated through thorough economic analyses to determine whether they are suitable for the establishment of collection centers. Additionally, a comprehensive vehicle routing problem is formulated to efficiently transport pharmaceutical waste from the constructed collection centers to waste and recycling centers or airports. Finally, the purpose of this model is to minimize the costs of the supply chain. The designed supply chain is shown in Figure 1.

3.1. Assumptions

(i) Each medicine has an expiration date and, after that, cannot be used.

(ii) The capacity of vehicles is determined.

(iii) Each place will be visited only once.

(iv) The number of pharmaceutical waste in each pharmacy is not more than the capacity of vehicles.

(v) The delivery time for pharmaceutical waste is instant.

(vi) The place of pharmacies, hospitals, disposal, and recycling centers are fixed, while there are several candidate locations for collection centers.

(vii) The cost of constructing collection centers is considered fixed.

(viii) The cost of commuting and transporting between each point by vehicle is determined.

(ix) Expired drugs include medications with a date of use under 1 year in pharmacy and other unused drugs returned by patients.

(x) Due to the low volume of reusable drugs, only one vehicle from collection centers is headed to airports to transport the medicines to developing countries.

3.2. Symbols and Signs in the Mathematical Model

3.2.1. Sets

I: The set of nodes of pharmacy and hospital

M: The set of distributors

R: The set of collection centers

N: The set of the union of pharmacies, hospitals, and collection centers

K: The set of existing vehicles in the collection of pharmaceutical waste's route (tour between pharmacy, hospitals, and collection points)

A: The set of disposal and recycling of pharmaceutical waste

H: The set of the union of disposal and recycling centers and collection points

L: The set of existing vehicles in a tour between collection points and disposal and recycling centers

F: The set of airports

P: The set of pharmacies and hospitals

UU_{rl}: The set of allocation of vehicles to the collection centers in the tour between the collection, recycling, and disposal points.

3.2.2. Indexes

$i \in P$, $p \in P$: Elements of the nodes of pharmacies and hospitals set

$r \in R$: Elements of the collection points set

$n \in N$, $n_1 \in N$: Elements of the set of the union of pharmacies, hospitals, and collection centers

$k \in K$: Elements of the set of existing vehicles in the route of collecting pharmaceutical waste

$a \in A$, $a' \in A$: Elements of the set of disposal and recycling of pharmaceutical waste

$h \in H$, $h' \in H$: Elements of the set of the union of disposal and recycling centers and collection points

$l \in L$: Elements of the set of the vehicle exist in the disposal of pharmaceutical waste routes

$f \in F$: Elements of the airport's set

UU_{l}: Elements of collection center's R, so that vehicle L belongs to them

$m \in M$: Elements of the set of distributors.

3.2.3. Parameters

MM: A vast number

dem_i: The existing amount of pharmaceutical waste in node i

Dem_p: Demand of pharmacies and hospitals

capV_k: Capacity of vehicle k

capD_r: Capacity of collection centers

capA_a: Capacity of disposal and recycling centers

capm_m: Capacity of distributors

RR_r: Coverage radius of collection centers

dd_{rf}: The distance between airport f and collection center r

cs_a: The cost of disposing and recycling

$\mathrm{vc'}_l$: The variable transportation cost between collection points and disposal, recycling points

$\mathrm{trebellow}_r$: The number of vehicles used for the collection of pharmaceutical waste

crf_{rf}: Transportation cost between collection points and airports

dis_{nn_1}: Distance between collection point and pharmacies or hospitals

$\mathrm{diss}_{hh'}$: Distance between collection points and disposal and recycling points

$\mathrm{treabove}_r$: The number of vehicles used for disposing of pharmaceutical waste

Price_r: Cost of construction of collection points

V_f: The amount of carbon dioxide that vehicles consume in the tour between collection centers and pharmacies and hospitals per unit distance and each unit of weight

$V_{f'}$: The amount of carbon dioxide that vehicles consume in the tour between collection centers and recycling and disposal centers, and airports per unit distance and each unit of weight

P_{co_2}: Cost per unit of carbon dioxide consumption

$\mathrm{Apercent}_r$: Percentage of pharmaceutical waste that is disposed

vc_k: Variable cost of the vehicle per unit of distance in a tour between collection center and pharmacies, and hospitals

fc_k: Fixed cost of transportation in a tour between collection center and pharmacies and hospitals

ffc_l: Fixed cost of transportation in a tour between collection center and recovery center.

3.2.4. Variables

zz_r: If the collection point is selected 1, otherwise 0

x_{nn_1k}: If there is a route from node n to node n_1 with the vehicle k_1, otherwise 0

aa_{pr}: If the node of pharmacy and hospital allocates to the collection point r_1, else 0

E_{arl}: If vehicle l of collection center r allocates to disposal node a, 1, else 0

yy'_{rf}: If medicines from collection point r transfers to the developing countries via airport f_1, if not 0

u_{al}: Variables to remove subtour in the route for disposing of medicines

ww_{nn_1k}: The amount of medicine shipped from node n to node n_1 is by vehicle k

$w_{hh'l}$: The amount of medicine that is transferred from node n to node n_1 is by vehicle l.

s_{ral}: The amount of pharmaceutical waste collected in the center a is emptied by vehicle l, which belong to the collection center r

$y_{hh'l}$: If there is a path from node h to node h' with vehicle l_1, otherwise 0

yy_{rf}: The amount of medicine transported from the collection center r to the airport f

yz_{mp}: The amount of medicine sent from the distributor m to the pharmacy p.

3.3. Mathematical Model

3.3.1. Objective Function. A single objective function is considered here, whose goal is to minimize supply chain costs. Costs like variable and fixed transportation costs, co_2 emission costs, construction of the collection centers costs, disposal, and recycling costs are addressed in this article.

3.3.2. Constraints.

$$Z = \min F. \tag{1}$$

The single objective function of the model.

$$F = f_1 + f_2 + f_3 + f_4 + f_5 + f_6 + f_7 + f_8 + f_9 + f_{10}. \tag{2}$$

F is the summation of the 10 different supply chain costs which descriptions are as followed:

$$f_1 = \sum_{r\in R} zz_r \cdot \text{price}_r. \tag{3}$$

The cost of construction of collection centers.

$$f_2 = \sum_{n\in N}\sum_{n_1\in N}\sum_{k\in K} \text{vc}_k \cdot \text{dis}_{n_1 n} \cdot x_{n_1 nk}. \tag{4}$$

The variable cost of transportation from collection centers to pharmacies and hospitals.

$$f_3 = \sum_{h\in H}\sum_{h'\in H}\sum_{l\in L} \text{vc'}_l \cdot \text{diss}_{hh'} \cdot y_{hh'l}. \tag{5}$$

The variable cost of transportation from collection centers to disposal and recycling centers.

$$f_4 = \sum_{a\in A}\sum_{r\in R}\sum_{l\in L} \text{cs}_a \cdot s_{ral}. \tag{6}$$

The cost of disposal and recycling of pharmaceutical waste.

$$f_5 = \sum_{n\in N}\sum_{n_1\in N}\sum_{k\in K} \text{dis}_{n_1 n} \cdot ww_{n_1 nk} \cdot v_f \cdot P_{\text{co}_2}. \tag{7}$$

The cost of emitted carbon dioxide due to the transportation between collection centers and pharmacies and hospitals.

$$f_6 = \sum_{h\in H}\sum_{h'\in H}\sum_{l\in L} \text{diss}_{hh'} \cdot w_{hh'l} \cdot v_{f'} \cdot P_{\text{co}_2}. \tag{8}$$

The cost of emitted carbon dioxide due to the transportation from collection centers to disposal and recycling centers.

$$f_7 = \sum_{k\in K}\sum_{r\in R}\sum_{n\in N} \text{fc}_k \cdot x_{rnk}. \tag{9}$$

The fixed cost of transportation between collection centers and pharmacies and hospitals.

$$f_8 = \sum_{l\in L}\sum_{r\in R}\sum_{h\in H} \text{ffc}_l \cdot y_{rhl}. \tag{10}$$

The fixed cost of transportation from collection centers to disposal and recycling centers.

$$f_9 = \sum_{r\in R}\sum_{f\in F} \text{dd}_{rf} \cdot \text{crf}_{rf} \cdot yy_{rf}. \tag{11}$$

The variable cost of transportation from collection centers to the airports.

$$f_{10} = \sum_{r\in R}\sum_{f\in F} \text{dd}_{rf} \cdot v_{f'} \cdot P_{\text{co}_2} \cdot yy_{rf}. \tag{12}$$

The cost of emitted carbon dioxide from transportation between collection centers and airports.

$$\sum_{n\in N}\sum_{k\in K} x_{pnk} = 1 \quad \forall p \in P \tag{13}$$

$$\sum_{n\in N}\sum_{k\in K} x_{npk} = 1 \quad \forall p \in P. \tag{14}$$

The previous and subsequent routes (the last and the next node) are set per node. It is essential to know that each node will be visited only once.

$$\sum_{n_1\in N} x_{n_1 nk} = \sum_{n_1\in N} x_{nn_1 k} \quad \forall n \in N,\ p \in P. \tag{15}$$

If any k-type vehicle enters each node, the exact vehicle must be got out of the node.

$$\sum_{n\in N} x_{rnk} + \sum_{n\in N} x_{npk} \le 1 + aa_{pr} \quad \forall p \in P, r \in R, k \in K. \tag{16}$$

According to each node's allocation to one of the collection centers. They must either be connected to the other node or the collection center.

$$\sum_{r} aa_{pr} = 1 \quad \forall p \in P. \tag{17}$$

Each node is allocated to just one collection center.

$$w_{rpk} = 0 \quad \forall p \in P,\ r \in R,\ k \in K. \tag{18}$$

No pharmaceutical waste is transported from the collection center to the first node, which is related to vehicle k.

$$ww_{ipk} \geq \sum_{n_1 \in N} ww_{n_1 ik} + \mathrm{dem}_i - \mathrm{MM} \cdot (1 - x_{ipk}) \quad \forall p, i \in P, k \in K. \tag{19}$$

Calculate the number of medicines vehicles k transfers from node p to a collection center.

$$\sum_{p \in P} aa_{pr} \cdot \mathrm{dem}_p \leq \mathrm{capD}_r \cdot zz_r \ \forall r \in R. \tag{20}$$

Determines the capacity of the collection center based on its chosen location.

$$\sum_{p \in P} aa_{pr} \cdot \mathrm{dem}_p \geq zz_r \ \forall r \in R. \tag{21}$$

If the collection center r is selected, then $aa_{pr} = 1$

$$ww_{npk} \leq \mathrm{capV}_k \ \forall p, \ i \in P, \ k \in K. \tag{22}$$

The amount of pharmaceutical waste collected by a vehicle should not exceed the vehicle's capacity.

$$\sum_{p \in P} \sum_{k \in K} x_{rpk} \leq \mathrm{trebellow}_r \cdot zz_r \ \forall r \in R. \tag{23}$$

Determines the desired number of vehicles for routing tours between the collection center and pharmacy and hospital for each collection center.

$$\sum_{h \in H} y_{ahl} = E_{arl} \ \forall a \in A, \ r \in \mathrm{UU}_l, \ l \in L, \tag{24}$$

$$\sum_{h \in H} y_{hal} = E_{arl} \ \forall a \in A, \ r \in \mathrm{UU}_l, \ l \in L. \tag{25}$$

Each node's entering and leaving routes per vehicle are determined based on the nodes assigned to the collection center.

$$u_{a'l} - u_{al} + \|A\| y_{a'al} \leq \|A\| - 1 \ \forall a, \ a' \in A, \ r \in R, \ l \in L. \tag{26}$$

The constraint of omitting the subtour.

$$\sum_{h' \in H} y_{h'hl} = \sum_{h' \in H} y_{hh'l} \ \forall n \in N, \ p \in P. \tag{27}$$

If vehicle l entered each node, the same vehicle l should leave that node.

$$\sum_{h \in H} y_{rhl} + \sum_{h \in H} y_{hal} \leq 1 + E_{arl} \ \forall a \in A, \ r \in \mathrm{UU}_l, \ l \in L. \tag{28}$$

Each node should connect to the other node or the collection center according to their allocation to one of the collection centers.

$$\sum_{a \in A} y_{rhl} \cdot \mathrm{MM} \geq \sum_{a \in A} E_{arl} \ \forall r \in \mathrm{UU}_l, \ l \in L. \tag{29}$$

Vehicle l goes to the next node from collection point r when the related vehicle and node are selected.

$$w_{ral} \geq \sum_{n_1 \in N} \sum_{k \in K} \left(ww_{n_1 rk} \cdot \mathrm{Apercent}_r \right) - \mathrm{MM} \cdot (1 - y_{ral}) \quad \forall r \in \mathrm{UU}_l, \ a \in A, \ l \in L, \tag{30}$$

$$w_{ahl} \geq \sum_{h' \in H} w_{ah'l} - \sum_{r \in \mathrm{UU}_l} s_{ral} - \mathrm{MM} \cdot (1 - y_{ahl}) \ \forall a \in A, h \in H, l \in L. \tag{31}$$

Determine the number of medicines each vehicle transfers from one node to the other.

$$\sum_{a \in A} \sum_{l \in \mathrm{UU}_r} s_{ral} = \sum_{n_1 \in N} \sum_{k \in K} ww_{n_1 rk} \cdot \mathrm{Apercent}_r \ \forall r \in R. \tag{32}$$

Determines the transfer value of each vehicle to the nodes based on the percentage of waste.

$$s_{ral} \leq E_{arl} \cdot \mathrm{MM} \ \forall r \in \mathrm{UU}_l, \ a \in A, \ l \in L, \tag{33}$$

$$s_{ral} \geq E_{arl} \forall r \in \mathrm{UU}_l, a \in A, l \in L. \tag{34}$$

If the variable E_{arl} equals to 1, then variable s_{ral} will get value.

$$\sum_{l \in L} \sum_{r \in \mathrm{UU}_l} s_{ral} \leq \mathrm{capA}_a \ \forall a \in A. \tag{35}$$

Determines the allocation capacity of each node.

$$\sum_{a \in A} \sum_{l \in \mathrm{UU}_r} y_{ral} \leq \mathrm{treabove}_r \cdot zz_r \ \forall a \in A. \tag{36}$$

The number of vehicles used in each collection center for routing pharmaceutical waste is determined.

$$\sum_{f \in F} yy_{rf} \leq \sum_{n_1 \in N} \sum_{k \in K} ww_{n_1 rk} \cdot (1 - \mathrm{Apercent}_r) \ \forall r \in R. \tag{37}$$

Determines the amount of medicine sent to airports.

$$\mathrm{RR}_r \cdot yy'_{rf} \geq \mathrm{dd}_{rf} \ \forall r \in R, \ f \in F. \tag{38}$$

If airports exist in the coverage area of the collection center, then the medicines will be sent to the airports.

$$yy'_{rf} \cdot \mathrm{MM} \geq yy_{rf} \; \forall r \in R, f \in F, \tag{39}$$

$$yy'_{rf} \leq yy_{rf} \; \forall r \in R, f \in F. \tag{40}$$

Determine the relation between 0 and 1 variable yy'_{rf} and the transferred amount of yy_{rf}.

$$\sum_{m \in M} yz_{mp} = \mathrm{Dem}_p \; \forall p \in P. \tag{41}$$

The amount of distributed medicines by distributors is the same as the demand of pharmacies and hospitals.

$$\sum_{p \in P} yz_{mp} \leq \mathrm{capm}_m \; \forall m \in M. \tag{42}$$

The amount of distributed medicines is not more than the capacity of the distributors.

$$x_{n_1nk}, \; zz_r, \; aa_{rk}, E_{arl}, \; yy'_{rf}, \; y_{hh'l} \in \{0, \; 1\}. \tag{43}$$

The abovementioned variables are the 0 and 1 variables.

$$ww_{nn_1k}, \; w_{hh'l}, \; s_{ral}, \; yy_{rf} \geq 0. \tag{44}$$

The variables above are positive.

4. Solution Approach

In this paper, in order to evaluate the performance of the proposed model and validate it, small-scale problems are solved by GAMS software using a CPLEX solver and then, sensitivity analysis was conducted to examine the robustness of the model to changes in parameters. Then, this problem was solved in small size using metaheuristic algorithms, particle swarm optimization (PSO), and genetic algorithm (GA), by MATLAB software to evaluate accuracy and validity of employed metaheuristic algorithms. Finally, for several medium- and large-scale problems, PSO and GA algorithms have been implemented using MATLAB software.

4.1. Particle Swarm Optimization. PSO is an optimization method that originated from the idea of computational intelligence, utilizing existing natural interactive systems. The concept was first developed by a social psychologist named Kennedy and an electrical engineer named Eberhart. The concept of PSO was inspired by the behavior of social animals such as bird flocks searching for food [51–53].

An algorithm based on PSO places particles at random in the search space in order to optimize a fitness function similar to that of a flock of birds in search of food. Each particle evaluates its quality or fitness at that position, and for a predefined number of iterations, each particle moves to a new location which gives a better fitness than the previous position. This movement is based on the particle's own history of best and current locations with those of the best positions attained by other particles in the swarm, with some random perturbations. In this manner, the swarm continues until it obtains the best solution to the fitness function in the problem space [51]. The fitness or objective function in PSO depends on the application area of the algorithm, and it is usually defined by a mathematical formulation to quantify the system performance achieved through a performance index. Unlike survival of the fittest, PSO is based on analogies with the social behavior of animals and birds. Unlike other evolutionary algorithms (EAs), there is no selection operation in PSO algorithm, and all the particles of the swarm are retained throughout the search process. Particle positions and velocities are updated in every iteration in accordance with the group's and the particle's best positions [54]. The fundamental algorithm for PSO involves a group of "n" particles, where each particle's position represents a potential solution in a D-dimensional search space. The particle's state is modified by three elements [55]:

(i) Its own inertia.
(ii) Personal most optimal position.
(iii) Swarm's most optimal position.

In PSO algorithm, the position and speed of the particles in the swarm change. In accordance with the following equations (6):

$$v_{id}^{k+1} = wv_{id}^{k} + c_1 r_1^k \left(\mathrm{pbest}_{id}^{k} - x_{id}^{k}\right) + c_2 r_2^k \left(\mathrm{gbest}_{id}^{k} - x_{id}^{k}\right), \tag{45}$$

$$x_{id}^{k+1} = x_{id}^{k} + v_{id}^{k+1}. \tag{46}$$

x_{id}^k and v_{id}^k represents position and velocity of i^{th} particle (out of n particles) at d-dimension in k^{th} iteration, respectively.

Best position and global best position (i.e., group's best) of i^{th} particle (out of n particles) at d-dimension in k^{th} iteration are represented by pbest_{id}^k and gbest_{id}^k. w represents inertial weight attached to the particle's previously attained position.

c_1 and c_2 represent acceleration constants.

r_1^k and r_2^k represent random numbers in the range of [0, 1].

Figure 2. shows the flowchart of PSO algorithm.

4.2. Genetic Algorithm. The GA is a type of search method that uses natural selection and genetics as a basis. It was created by John Holland in the 1970s and involves starting with a group of solutions, known as a population, represented by chromosomes. The fitness of each chromosome is evaluated and the next generation is created based on their fitness values, with some selected chromosomes mating and producing offspring through crossover and mutation. The population size remains the same throughout the process, and the algorithm continues to repeat until the end condition is met [56–58].

A GA is a type of search method used in computing to find approximate or exact solutions to search and optimization problems. It is considered a global search heuristic and a subcategory of EAs. GAs draw inspiration from evolutionary

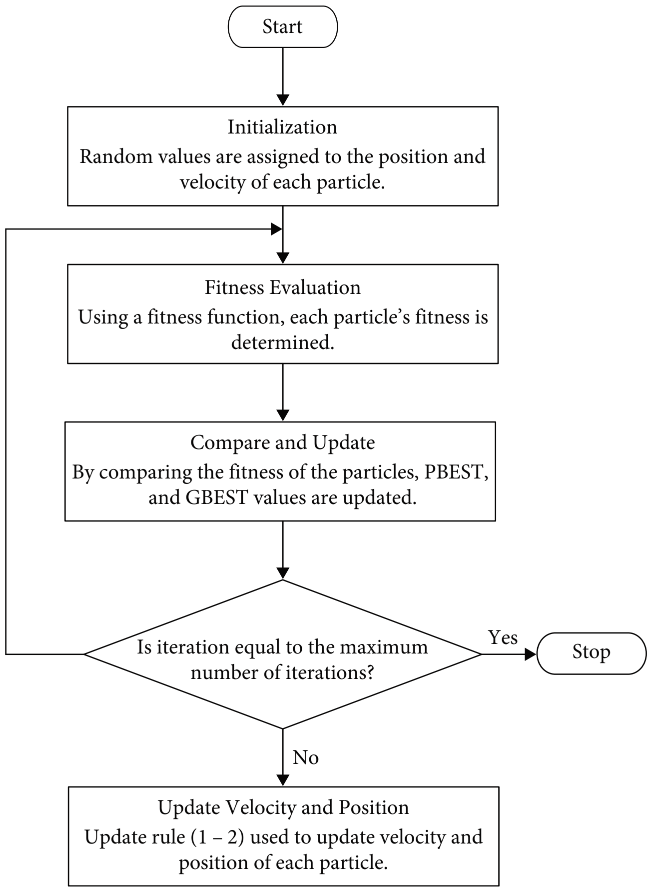

Figure 2: Flowchart of PSO [52].

biology and use techniques such as inheritance, mutation, selection, and crossover to find optimal solutions to complex problems in various fields like biology, engineering, computer science, and social science. EAs, including GAs, are used to solve problems that lack a well-defined and efficient solution. GAs have been applied successfully to solve optimization problems such as scheduling and shortest path, and to model systems with random elements like the stock market [56].

The GA methodology is comprised of four main parts, namely initialization, selection, reproduction, and termination. The initial population is formed by generating a large number of individual solutions at random during the initialization phase. The size of the population depends on the nature of the problem. Solutions may also be placed in areas where optimal solutions are likely to exist [56].

During the selection phase, a portion of the existing population is chosen to breed the next generation. Individual solutions are selected based on fitness, where solutions with a higher fitness value are more likely to be chosen. There are various selection methods that may be used to determine the fitness of each solution or a random sample of the population. In order to maintain population diversity and prevent premature convergence, stochastic functions select a small number of less fitting solutions. Roulette wheel selection and tournament selection are two well-known selection methods. As a method of selection, roulette wheel selection is used in this paper [56].

Input:
Population size (n)
Maximum number of iterations (MAX)
Output:
Global best solution, Y_{bt}
Begin
 # Create an initial population of n chromosomes Y_i *(i = 1, 2,…, n)*
For i = 1 to n
Y_i *= generate_chromosome()*
compute_fitness(Yi)
Set iteration counter t = 0
While (t < MAX)
A selection of two chromosomes is made from the initial population based on fitness
Apply crossover operation on selected pair with crossover probability
Apply mutation on the offspring with mutation probability
Replace old population with new offspring
Increase the current iteration t by one.
end while
return the best solution found, Y_{bt}
end

Algorithm 1: Genetic Algorithm (GA).

In the reproduction phase, a second generation population of solutions is generated using genetic operators such as crossover and mutation. For each new solution, a pair of parent solutions is chosen from the previously selected pool. Crossover functions on part portion of genes from parent chromosomes which results in creation of a new offspring. The purpose of mutation is to prevent all solutions in a population from falling into a local optimum of the solved problem. Offspring results from crossover randomly changes by mutation operation. By creating a child solution using crossover and mutation methods, a new solution is produced that shares many characteristics of its parents. This process continues until a new population of appropriate size is created [56, 59, 60].

The termination phase involves repeating the generational process until a termination condition is met. In this paper, maximum number of iterations is used as termination condition. This results in a new population of chromosomes that is different from the initial population, with an increase in average fitness due to the selection of the best solutions from the previous generation along with some less fit solutions to maintain diversity [56].

Algorithm 1 shows the pseudocode of GA [61].

4.3. Parameters. Algorithm parameters for each PSO and GA are as follows in Tables 2 and 3.

The problem parameters of this research are set based on the articles and sources available in this field and based on random experiments. They are shown in Table 4.

Table 2: Parameters considered in the GA algorithms.

GA		
Maximum number of iterations	MaxIt	100
Population size	nPop	100
Crossover size	pc	0, 9
Number of offspring (parents)	nc	2*round (pc*nPop/2)
Mutation percentage	pm	0, 1
Number of mutants	nm	Round (pm*nPop)

Table 3: Parameters considered in the PSO algorithms.

PSO		
Maximum number of iterations	MaxIt	100
Population size (swarm size)	nPop	120
Inertia Weight	w	0, 3
Interia weight damping ratio	wdamp	0, 99
Personal learning coefficient	c_1	2, 5
Global learning coefficient	c_2	0, 7

Table 4: Problem parameters.

Parameters	Unit	Parameter distribution
Coverage radius of collection centers	km[1]	U (15, 80)
Distance between collection points and pharmacies or hospitals	km	U (1, 20)
Distance between a pharmacy or hospital and another pharmacy or hospital	km	U (0.1, 2)
A vast number		100,000
The capacity of disposal and recycling centers	kg[2]	U (20, 60)
Percentage of pharmaceutical waste that is disposed		U (0.5, 1)
Number of vehicles used for the collection of pharmaceutical waste		Round (U (1, 4))
Number of vehicles used for disposing of pharmaceutical waste		Round (U (1, 4))
Cost of disposing and recycling	Mt[3]	U (0.0001, 0.0004)
The variable cost of the vehicle per unit of distance in a tour between collection centers and pharmacies, and hospitals	Mt	U (0.01, 0.02)
Fixed cost of transportation in a tour between collection centers and pharmacies, and hospitals	Mt	U (7, 18)
The demand for pharmacies and hospitals	kg	Round (U (30, 60))
The capacity of vehicle k	kg	U (100, 150)
The capacity of collection centers	kg	U (200, 300)
Capacity of distributors	kg	U (200, 400)
Cost of construction of collection points	Mt	U (100, 300)
Cost per unit of carbon dioxide consumption	Mt	U (3, 7)
Amount of carbon dioxide that vehicles consume in the tour between collection centers and pharmacies, and hospitals per unit distance and each unit of weight	kg	U (0.2, 1)
Amount of carbon dioxide that vehicles consume in the tour between collection centers and recycling and disposal centers, and airports per unit distance and each unit of weight	kg	U (0.1, 0.99)
Distance between collection points and disposal and recycling points	km	U (30, 100)
Distance between disposal and recycling centers	km	U (30, 100)
The variable cost of the vehicle per unit of distance in a tour between collection centers and recycling and disposal centers	Mt	U (0.1, 0.4)
Fixed cost of transportation in a tour between collection centers and recovery centers	Mt	U (10, 30)
Distance between airport f and collection center r	km	U (200, 245)
Transportation cost between collection points and airports	Mt	U (20, 30)
Existing amount of pharmaceutical waste in pharmacies and hospitals	kg	$dem_i = (l, m, u)$ l~U (1, 2) m~U (3, 4) u~U (5, 7)

[1]Kilometer, [2]Kilogram, [3]Million toman (currency of Iran).

5. Solving the Proposed Model in Small-Scale Problems Using Gams Software, GA, and PSO Algorithms

In this section, three small-scale case studies are analyzed utilizing CPLEX solver (branch and bound algorithm) in GAMS software, GA, and PSO to assess their performance in solving the problem. The results of these case studies are presented in tabular form and compared in terms of the objective function values obtained by each method. This comparison allows for a comprehensive evaluation of the efficiency and effectiveness of CPLEX solver in GAMS, GA, and PSO in addressing the problem under consideration.

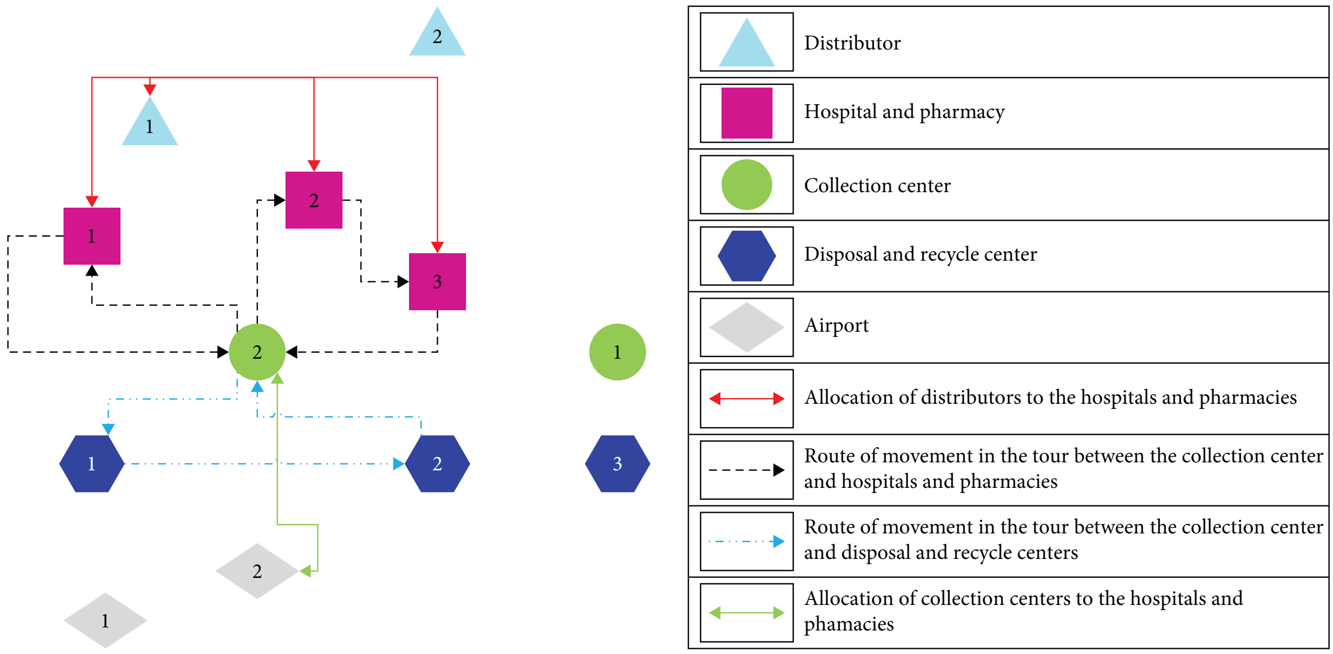

FIGURE 3: The network for the first example.

For example, in the first small-scale problem, the issue is implemented for two distributors, two collection centers, three pharmacies and hospitals, three places for disposal and recycling, and two airports. Figure 3 is the schematic of the first example.

According to the example schematic, despite two candidate locations for the collection center, only one collection center has been constructed due to its economic examination. Moreover, only one distributor was sufficient to deliver the medicines to three points of hospitals and pharmacies, and there was no need to use a second distributor. We considered three recycling and disposal centers in this model, but two were chosen. Moreover, reusable medicines were sent to only one airport. The result of the first small-scale problem and the two others are mentioned in Tables 5 and 6.

The second example has implemented the issue for two distributors, two collection sites, four pharmacies and hospitals, four places for disposal and recycling, and two airports. The third example has implemented the issue for three distributors, two collection sites, four pharmacies and hospitals, four places for disposal and recycling, and four airports. Table 7 exhibits the outcomes derived from the application of GAMS, GA, and PSO in the aforementioned examples. The deviation between the exact solution obtained from GAMS and the solutions derived from the metaheuristic approaches, namely PSO and GA, is below 7%. This indicates that the metaheuristic algorithms have produced satisfactory results.

6. Sensitivity Analysis

To further understand the performance of the proposed model, a sensitivity analysis of the parameters affecting the cost has been performed, and the changes of the objective function based on the changes of the mentioned parameters in the model are investigated based on the information of the fourth example. The results are shown in Table 7.

In order to perform the sensitivity analysis, because the capacity of disposal centers is one of the factors determining whether the model can be done or not, as a result, we analyze the model by changing the parameters of node a_1 capA_{a_1}. When we increase it, due to the rise in the capacity of the disposal center and the lower cost of disposing of that center compared with the costs of other centers, the model tries to allocate more waste to this center (taking into account other costs). Therefore, this increase leads to a decrease in other costs like transportation and environmental costs. Finally, the whole objective function will be dropped when other costs decrease. Table 8 demonstrates the changes in objective function based on the changes in the capacity of the disposal center.

The cost $\mathrm{crf}_{r_1 f}$ will play a significant role in the model due to the influence of allocating the hospital location to the desired depot for sending medicines to airports (developing countries). As a result, with the increase in the cost of the first depot, the allocation of hospitals to those depots decreases until a balance between the increase of this cost and other costs according to the objective through the number and diversity in the allocation of different hospitals, leading to a reduction in the cost of transferring from the depot to the airport location (developing countries). Moreover, reducing the total cost, on the other hand, reducing this cost ($\mathrm{crf}_{r_1 f}$) will lead to the allocation and diversity of more hospitals to this depot to reduce the total costs of the target functions.

Table 5: The result of implementing the model for the first example in GAMS, GA, and PSO.

First example											
Algorithm		Vehicle	Routes	Distributor	Pharmacy and hospital		Collection center	Airport		Solving duration	Result of objective function
					p_1	p_2		f_1	f_2		
GAMS	The route between collection centers and hospitals and pharmacies	k_1	r_1 p_2 r_1	m_1	20	15	r_1	0	4.5	1.042 s	55,395.48
		k_2	r_2 p_1 r_2								
	The route between collection centers and recycling and disposal points	l_1	r_1 a_1 r_1				r_2	4	0		
		l_2	r_2 a_2 r_2								
GA	The route between collection centers and hospitals and pharmacies	k_1	r_2 p_1 p_2 r2	m_1	3.4057	15	r_2	7.2894	6.9993	8.542 s	55,589.67
	The route between collection centers and recycling and disposal points	l_2	r_2 a_1 r_2	m_2	16.5943	0					
PSO	The route between collection centers and hospitals and pharmacies	k_1	r_2 p_1 p_2 r2	m_1	9.9922	9.9922	r_2	0.0014	6.9986	9.8137 s	55,591.45
	The route between collection centers and recycling and disposal points	l_2	r_2 a_1 r_2	m_2	10.0574	5.0078					

Table 6: The result of implementing the model for the second example.

	GAMS		GA		PSO	
Example	Objective function	Solving duration	Objective function	Solving duration	Objective function	Solving duration
2	104,907.8	1.49 s	110,807	8.9385 s	111,492.2	10.2819 s
3	187,743.1	3.35 s	183,344.7	8.9082 s	185,460.2	10.4789 s

Table 7: Sensitivity analysis for the capacity parameter of node a_1.

Parameter	Changes in the capacity of the disposing center	Disposal cost in a_1	Objective function
	+50%	8,121.353	158,710
	+20%	6,497.083	163,890
capA_{a_1}	0	5,414.236	168,630
	−20%	4,331.389	170,750
	−35%	3,519.253	171,600

Table 8: Sensitivity analysis for the transportation cost parameter between the collection center and the airport.

Parameter	Changes in the cost of transportation from the first depo to the airport	Allocated amount from hospital to the first depo	Objective function related to the cost of the transportation from the first depo to the airport	Objective function
	+50%	1	97,178.142	180,070
	+20%	1	90,531.739	173,420
$\text{crf}_{r_1 f}$	0	2	89,386.585	168,630
	−20%	2	83,478.671	162,730
	−35%	2	70,956.823	150,050

Table 9: The number of sets considered in medium and large examples.

Example	Sets				
	|P|	|A|	|F|	|M|	|R|
4	5	4	3	3	3
5	6	5	3	4	4
6	7	6	4	5	5
7	8	8	5	6	6
8	10	10	6	6	6

Table 10: The result obtained from the execution of algorithms for problems with large examples.

Example	GA		PSO	
	Objective function	Solving duration	Objective function	Solving duration
4	168,861.4272	18.7259	169,246.001	23.3391
5	173,631.1846	18.7671	180,015.735	22.5382
6	214,571.382	22.4777	238,912.132	31.0459
7	355,649.5141	24.3952	371,432.312	31.1444
8	583,891.7895	25.9036	547,771.199	33.1042

7. Solving Medium- and Large-Scale Problems Using GA and PSO

Table 9 shows the amount of each set considered for the examples that need to be implemented in the metaheuristic algorithms.

In Table 10, there is the information that is extracted from the implementation of the meta-heuristic algorithms for examples 4–8.

8. Managerial Insights

Managers' viewpoints in each field are one of the main factors in the success of a system. In a system like the PSC, where the cost of production is high, and waste is hazardous, reducing the waste and improving the chain's productivity are considered the management focus. In this article, we create a model which ensures that medicines are used unless they do not have an expiration date; this approach not only decreases the waste but also lowers the demand for medicines and thus helps the drug industry to produce less. This model also guarantees that the wastes are appropriately treated (recycled or disposed of). This article also allows managers to pay less tax than regular tax. In some countries, when a company does some charity activity, the government offers them discounts on their taxes. With this model, drugs with an expiration date will be sent to the airports to transfer to developing countries whose people cannot afford to buy medicines. With this action, the level of health in developing countries will be increased, influencing the whole world's health. As a result, this article aids managers in improving their performance.

9. Conclusion

Environmental and economic issues are among the most critical concerns in modern society. Numerous reputable companies worldwide strive to improve their ecological image in addition to enhancing the quality of their products and services. The current study addresses the issue of pharmaceutical waste management and the reduction of carbon dioxide emissions by finding the optimal location for establishing collection centers and identifying optimal routes. The proposed approach aims to contribute to the environmental image of the implementing company while also reducing costs incurred throughout the chain. The present study tries to simulate and optimize a multilevel PSC with the aim of minimizing various expenses of the entire chain associated with transportation, construction, and allocation by developing a mathematical model for small- and large-scale scenarios. Metaheuristic algorithms such as GA and PSO have been applied to this problem to identify the optimal locations for collection centers and routes for vehicle transportation between collection centers, hospitals, pharmacies, and disposal/recycling centers. Additionally, the study seeks to determine the appropriate allocation of medicines from distributors to pharmacies or hospitals, as well as the allocation of reusable drugs from collection centers to airports. The study finds that the GA algorithm generally outperforms the PSO algorithm regarding both computational efficiency and solution quality. In this study, the GA and PSO algorithms were found to produce high-quality solutions in a short amount of time. These algorithms produced results close to those of the exact solution algorithm, particularly in small-scale problems.

Advanced optimization algorithms have proven highly effective in solving complex problems in various domains, including online learning, scheduling, multiobjective optimization, transportation, medicine, data classification, and more. These algorithms are designed to find the optimal solution among a large number of possible solutions, often in a highly constrained environment. Their ability to handle complex decision-making problems with many variables and constraints has made them highly popular in many applications. In recent years, there has been growing interest in applying optimization algorithms to address complex optimization problems.

One of these types of algorithms is the metaheuristic algorithm. In the realm of optimization problems with high-dimensional search spaces, exact optimization algorithms may not be a viable solution. This is because the search space exponentially increases with problem size, and exhaustive search is impractical. Furthermore, classical approximate optimization methods, such as greedy-based algorithms, may require certain assumptions that are difficult to validate for each problem. As a result, metaheuristic algorithms have gained prominence in solving optimization problems due to their ability to search through vast candidate solution spaces without requiring many assumptions about the problem. Population-based metaheuristic algorithms, in particular, are ideal for global searches as they possess both global exploration and local exploitation capabilities [62]. These algorithms are capable of handling complex optimization problems with multiple objectives and constraints. They work by iteratively exploring the search space and identifying candidate solutions that are improved upon in each iteration until a satisfactory solution is found. These algorithms are capable of finding optimal or near-optimal solutions, which are essential for decision-makers in location–allocation, routing, and scheduling problems because these problems are often complex, with various multiobjective and single-objective structures. Therefore, finding the exact optimal solution using exact algorithms can be time-consuming. In recent years, various advanced optimization algorithms based on heuristic and exact methods have been proposed, with many achieving impressive results, including but not limited to simulated annealing, GA, PSO, ant colony optimization, artificial bee colony algorithm, harmony search algorithm, and many others [63–69]. Besides, several recent studies have explored the combination of exact and heuristic algorithms in order to achieve an acceptable result in terms of both time efficiency and a good solution, such as hybridizing GAs with branch and bound techniques, branch and bound-PSO hybrid algorithms [63, 64].

Therefore, future research could explore more complex and advanced optimization algorithms methods to improve upon the results of the present study. For example, Dulebenets [65] proposes a new algorithm called adaptive polyploid memetic algorithm for scheduling cross-docking terminal trucks. It relies on the polyploidy concept to store copies of parent chromosomes for crossover operations. The algorithm uses problem-specific hybridization techniques to improve solution quality and outperforms state-of-the-art metaheuristics. To solve problems of spatially constrained berth scheduling, Kavoosi et al. [66] proposes an island-based metaheuristic algorithm (UIMA). The UIMA population is divided into four subpopulations, with four different population-based metaheuristics, including EA, PSO, estimation of distribution algorithm, and differential evolution, used to search each island. Various operators are incorporated into the metaheuristics, which aid in the discovery of better results. Moreover, in paper [68] a novel EA is created to solve a mathematical model using an augmented self-adaptive parameter control strategy. The algorithm's parameters are adjusted throughout the search process. It is compared with nine other meta-heuristic algorithms that are commonly used for berth scheduling in marine container terminal operations.

In terms of problem structure and attributes, future research could consider incorporating pharmaceutical waste uncertainty into the model to enhance its applicability to real-world problems. Additionally, different types of VRPs, such as VRPs with a time window and long-distance ps, could be explored. Adopting different vehicle types based on the capacity of each collection point can also help reduce costs. Overall, the study offers insights into optimizing pharmaceutical waste management and can help organizations make informed environmental and economic sustainability decisions.

Consequently, this paper can benefit companies operating in this field, as well as the government, from both economic and environmental perspectives.

Data Availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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