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A new bi-objective green medicine supply chain network design under fuzzy environment: Hybrid metaheuristic algorithms

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ABSTRACT

This paper studies the design of the green medicine supply chain network under uncertainty, which integrates allocation, location, production, distribution, routing, inventory, and purchasing problems. The main contribution of the current paper is to design a fuzzy bi-objective Mixed-Integer Linear Programming (MILP) model for a multi-period, three-echelon, multi-product, and multi-modal transportation green medicine supply chain network (GMSCN). Additionally, the main aim of this network is to consider the environmental impacts related to the establishment of pharmacies and hospitals, by focusing on the reduction of greenhouse gases and the control of environmental pollutants. Therefore, to cope with uncertain parameters, fuzzy programming is utilized to examine uncertainty parameters. To solve the GMSCN model, meta-heuristic algorithms are used, including social engineering optimization, improved kill herd, improved social spider optimization, and hybrid whale optimization and simulated annealing. In this regard, two new hybrid algorithms called hybrid Firefly Algorithm and Simulated Annealing (HFFA-SA) and Hybrid Firefly Algorithm and Social Engineering Optimization (HFFA-SEO) to solve the proposed model for the first time are developed. In order to show the applicability of our paper and the lack of benchmark functions in the literature, a set of simulated data in two sizes including small- and large-sized problems is provided. Finally, the results of the analysis and the designed problems indicate that the GMSCN model and developed solution approaches are promising.

1. Introduction

The medicine industry is defined as a system of organizations, processes, and operations include in the discovery, production, and development of medicines. The Medicine Supply Chain (MSC) is a way in which medical products with proper quality at a proper place and time between receivers and consumers are distributed (Uthayakumar & Priyan, 2013). The MSC is considered an imperative global industry, given the impact on human life, any problem in the access to medicine items during a high-volume distribution and production can endanger the lives of people. In developed communities, the state of health is distinguished as an important criterion, which is directly linked to the time and sufficient supply of vital medicines (Bouziyane, Dkhissi, & Cherkaoui, 2020; Haghjoo, Tavakkoli-Moghaddam, Shahmoradi-Moghadam, & Rahimi, 2020; Taghipour, 2014; Azzaro-Pantel, 2018). To reach the highest state in the health care system of a country, it is necessary to predict the amount and the order of the required drug during the in-need time (Priyan & Uthayakumar, 2014; Azzaro-Pantel, 2018). Keeping this point in mind that the process of distributing and supplying medicines is not only influenced by the functioning of an organization or institution, but also depends on a chain of institutions that contribute to the performance of this procedure. Through the last years, the medicine market has not only been rising, but also expanded in range and variety. So, the importance of MSC has called further notice. In this regard, the optimization methods have been voraciously applied to these types of networks to satisfy consumers' needs optimally (Taghipour & Frayret, 2013; Priyan & Uthayakumar, 2014; Tliche et al., 2019; 2020).

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The MSCs' growth and complexity pose some problems for the distribution of vital medicines and elements. One of the main topics in the field of health is related to the drug distribution system. The essential parts of the medical distribution system are pharmacies (drug distribution centers) in hospitals (health centers). At the same time, it is the responsibility of pharmacies to deliver the medicine to all parts of the health center and the individual. These days, with the swift growth of the industry in the world, the environmental problem and the effects of ecology on products have become a significant problem (Farias et al., 2020; Krim et al., 2020). Serious concerns about the environmental impacts and increased risks posed by industrial activities to the health of humans have led to raising researches in the field of Green Supply Chain (GSC) management. Based on the fast-paced industrialization of the world, and the environmental impact of commodities, the topic of the GSC has been taken into further consideration. The GSC is one of the best solutions to protect the environment, industries, transportation systems, and improve the current conditions on Earth. One of the most essential differences in the MSC and GSC is the addition of the green concept to environmental impacts, but what enters into the MSC structure is something beyond environmental concerns. In other words, GSC management not only addresses environmental concerns in the supply chain, but also considers productivity and increased profits (Loivet et al., 2020; Govindan et al., 2014; Pasandideh et al., 2015; Soares et al., 2020; Xu et al., 2020; Ahmadini et al., 2021). In this regard, transportation systems are utilized to deliver and distribute medicines and other essential materials. So, choosing a vehicle (based on the cost and capacity associate with environmental effects such as the amount of fuel and gas generated by carbon dioxide per unit of mileage) can affect the type of vehicle choice. Today, transportation systems generate about 27% of greenhouse gas emissions of the world (Wong et al., 2020; Goswami et al., 2020; Zhang & Yousaf, 2020; Cauchois et al., 2017). According to the aforementioned reasons, proper performance and choosing a transportation system would affect the time of delivery, operating costs, quality of service, energy consumption reduction, and facility utilization.

In the reviewed problems, in references, Susarla and Karimi (2012), Mousazadeh et al. (2015), Bijaghini and SeyedHosseini (2018), Zahiri et al. (2018), and Limbourg and Jourquin (2009), the problems of procurement-distribution-production, location-distribution-allocation, routing-inventory-production, and production-distribution-routing are provided simultaneously (Mbiatem et al., 2018). However, a new production-distribution-allocation-routing-purchasing-inventory holding-ordering problem in this work is provided (Lättilä et al., 2013). Additionally, the challenge of the environmental effects (CO_2 emission) is considered in the Green Medicine Supply Chain Network (GMSCN) for the first time in this paper. In this regard, in the investigated papers, for instances, in works Hansen & Grunow, 2015; Lai, Ngai, & Cheng, 2002; Roshan, Tavakkoli-Moghaddam, & Rahimi, 2019; Singh & Goh, 2019; Vishwakarma, Garg, & Barua, 2019, and Priyan and Mala (2020) is not addressed the issue of the environmental impacts or carbon dioxide gas emission. The current paper aims to present a new multi-product multi-period three-echelon model for GMSCN associate with environmental impacts and the control of environmental pollutants under uncertainty. Then, a new bi-objective MILP model considering multi-modal transportation is formulated. Therefore, multi-modal transportation is the most critical and vital factor in the economic system of the GMSCN, so that, further of the costs in the proposed model would be related to this system. The main aims of this network are to minimize the total costs and environmental impacts.

To investigate uncertainty-related studies include Mousazadeh et al. (2015), El Mokrini et al. (2016), Zahiri et al. (2017), and Zahiri et al. (2018) are addressed a robust-possibilistic technique, PROMETHEE and fuzzy AHP methods, fuzzy possibilistic-stochastic programming method, and robust-possibilistic strategy respectively. Moreover, in this paper, in the terms of inventory holding and transportation costs are considered as the uncertainty parameters in the GMSCN model. To handle the uncertainty parameters, a fuzzy approach for the GMSCN is provided. Based on the complexity and NP-hard of the GMSCN model, the CPLEX procedure is used to solve the model in small-sized problems. Another novelty of this paper the proposed solution methodology. Then, to solve the presented model, Social Engineering Optimization (SEO), Improved Kill Herd (IKH), Improved Social Spider Optimization (ISSO), and Hybrid Whale Optimization and Simulated Annealing (HWO-SA) algorithms are used. In this regard, two novel hybrid metaheuristic algorithms, namely, Hybrid Firefly Algorithm and Simulated Annealing (HFFA-SA) and Hybrid Social Engineering Optimization and Firefly Algorithm (HSEO-FFA) are developed to solve the suggested model for the first time.

In this paper, a bi-objective MILP model is developed to minimize both the total cost and environmental effects. The main contributions of this paper, which differentiates our study from the existing literature are as follows (further explanation can be found in Section 2):

- Designing a multi-period multi-product multi-echelon green medicine supply chain network with uncertainties in transportation and inventory holding costs;
- Developing a bi-objective MILP model to design an integrated GMSCN which aims at optimizing network total costs and environmental aspects simultaneously;
- Considering the multi-modal transportation in the proposed model;
- Integrating production, allocation, location, routing, inventory holding, distribution, and purchasing problems into the green medicine supply network design model;
- Proposing a fuzzy programming approach to cope with the uncertainty of the input parameters;
- Developing two new hybrid meta-heuristic algorithms to solve the proposed model for the first time.

The outline of the paper is as follows: Section 2 states related works and researches, relevant papers in GMSCN, and metaheuristic algorithms. In Section 3, a detailed description and mathematical formulation of the presented model along with the assumptions, and fuzzy programming approach are proposed. In addition, the presented solution method is introduced in Section 4. The computational results, numerical examples, managerial insights, and sensitivity analysis that illustrate the performances of the presented model and algorithms are explained in Section 5. Finally, the conclusion and future works are investigated in Section 6.

2. Literature review

The literature review can be categorized into two main subgroups: MSCN models and meta-heuristic algorithms. According to the novelty of the MSCN model, there are a few papers in this field of study.

3. MSCN models

In this sub-section, studies examine related to the MSCN models Sousa et al. (2005) addressed an allocation-distribution model of a multi-period multi-product MSCN. To solve the model a Lagrangian decomposition approach and a heuristic algorithm, where frames of commodities are optimized sequentially, are utilized. Susarla and Karimi (2012) developed an integrated procurement-production-distribution model along with international tax differential effects, material shelf-lives, inventory holding costs, real-life factors, and waste treatment/disposal for a multi-period enterprise-wide planning MSCN. Also, a new MILP mathematical model is formulated. Two instance problems of planning multi-national pharmaceutical companies to solve the efficiency of their model is provided. Mousazadeh et al. (2015) presented an allocation-distribution- location problem for the MSCN. Additionally, a bi-objective MILP model along with minimizing total costs and unfulfilled demands is designed. A robust possibilistic method to cope with uncertain parameters is provided. A case study to validate the model is used and managerial insights are provided. Hansen and Grunow (2015) developed a two-echelon MSCN under stochastic demand by using collaborative decision-making. A case, according to an empirical study for the model is applied. Then, an instance of how quantitative methods can propose worthwhile decision support for commodity launch operations is provided. Weraikat et al. (2016) explored the providing incentive role to customers to improve sustainability and to facilitate leftover returns for a MSCN. Also, a planning, allocation, and distribution operations problem for balancing risks and time-to-market in the MSCN is provided. Furthermore, the effect of having a suitable coordination approach among responsible for collecting unwanted medications from customer zones, a third-party logistics and producer of medications is investigated. An approach to share the MSC saving between the third-party logistics firms and the producer is proposed. El Mokrini et al. (2016) addressed the evaluating the feasibility of outsourcing to enhance the efficiency of their supply chain in the pharmaceutical supply chain (PSC). To tackle uncertainty and difference risks in the PSC, a heuristic method for risk assessment is proposed. PROMETHEE and fuzzy AHP methods to assess risks and allocate them to predefined categories are combined. Also, an application to the PSCs is provided to show the efficiency and quality of the approach. Nematollahi et al. (2017) investigated simultaneous coordination of visit service level and intervals in a bi-level PSC along with stochastic demand. Both members' conditions for participation in the collaboration models are provided. Then, a model to the case of collaboration on satisfying the needed fill rate in two different scenarios (social and economic collaborative decisions-making) in PSC is extended. Several test problems are carried to compare the efficiency of various decision-making structures. Zahiri et al. (2017) designed a novel bi-objective integrated sustainable-resilient MILP model for the PSCN under uncertainty as well as introduced novel measures for sustainability and resiliency. A novel fuzzy stochastic-possibilistic programming approach to tackle with the uncertain parameters is extended. Additionally, a novel meta-heuristic algorithm and also a new Pareto-based lower bound approach are developed to solve the NP-hard nature of the problem. A case study and several experiment problems for the LGBTQ community are addressed. Mehralian et al. (2017) addressed a coordination structure among producing and delivering the proper product to the right people at the suitable time of PSC member. Moreover, recognizing and prioritizing the factors affecting the coordination of a PSC was the aim of their study. The analytic hierarchy process method to prioritize six strategic criteria is employed. Bijaghini and SeyedHosseini (2018) extended a new bi-echelon bi-objective, inventory, production, and routing problem for a MSCN. The aim of the model was to make a proper trade-off among the budget cost and customer satisfaction. A MILP model under uncertainty has been formulated where objective functions are the minimization of the budget during the scheduled time and the shortage amount associated with the lost sale of drug demands delivering of medicine stores. Hence, the robust method to handle the uncertainty parameters is considered and also a Benders decomposition algorithm to solve the problem is used. The results of the model are indicated that the model causes an improvement in the MSCN. Zahiri et al. (2018) presented a new production, distribution, and routing model for bi-objective MSCN problem by considering products substitutability, quality discount, and perishability under uncertainty. Two objective functions include to decrease the total cost and to increase unmet demand are provided. Then, a robust possibilistic technique to handle the uncertain parameters is introduced. Therefore, a case study to validate the network is provided. Vishwakarma et al. (2019) challenged the pharmaceutical supply chain by the barriers in the context of developing countries such as India. To improve the efficiency of the pharmaceutical industry, the identification of barriers is desired, which is identified 28 barriers under six main criteria. A hybrid model according to the fuzzy AHP to prioritized rank barriers in the medical industry is developed. Roshan et al. (2019) addressed crisis management in the MSC that three objective function i.e., the minimization of the total costs, the minimization of the unmet demand, and the maximization of the satisfaction of social responsibility are addressed. Also, substitutability and perishability along with demand uncertainty is considered. Moreover, two methods, i.e. TH and Me, are used to cope the uncertainty and the multi-objective model. A case study to validate the mathematical model is presented. Weraikat et al. (2019) developed a new mathematical model to explore the effect of implementing a Vendor-Managed Inventory system along with the minimization of the quantity of the expired medications at hospitals. Hence, a mixed-integer nonlinear programming model for MSCN problem is designed. Moreover, several Monte-Carlo simulation experiments are conducted to evaluate the robustness of the model under demand uncertainty. A case study under deterministic demand indicates the performance of the model in eliminating the amount of expired medicines without compromising the satisfaction of the customers. Singh and Goh (2019) formulated an application and a multi-objective MILP model under uncertainty for an MSCN. An intuitionistic fuzzy method to cope with the uncertainty of the main parameters is represented. First of all, their model is converted into a crisp MILP model by utilizing proper defuzzification strategies. By using two scalarization techniques, *i.e.* the minimum bounded sum operator and the gamma-connective techniques, the model is converted into a single objective model. A set of experimental problems to solution methodology and a multi-objective MSCN model along with self-generated random data are applied. Priyan and Mala (2020) suggested a game theory method to address inventory strategies for managing the flow of a medical raw-material incorporating various quality features in a bi-level medical industry supply chain and hospital. A realistic situation where the deteriorating rate of a finished product gently raises as the expiration date methods is considered. Also, a procedure to decide an optimal strategy for achieving the objective customer service level of the hospital with the support of the game theory payoff matrix is designed. Moreover, a set of experimental problems to demonstrate the solution methodology and the sensitivity analysis of the main parameters to illustrate the model are provided. Zandkarimkhani et al. (2020) designed a pharmaceutical supply chain network under uncertainty. They formulated a bi-objective, multi-product multi-period MILP model for location-inventory-routing problems. Their aims of their model were to minimize the total costs and lost demand amount. To cope with uncertain parameters, chance-constrained programming and goal programming methods are used.

3.1. Meta-heuristic algorithms in MSCN models

Some of the literature on MSCN problems only used exact solution approaches such as Lagrangian relaxation, branch and bound, benders decomposition algorithm, etc. to deal with SCND problems. On the other hand, because of the limitation of these exact methods to tackle NP-hard problems on a large-scale, there are other papers in the field of MSCN, which employed meta-heuristic algorithms to deal with these problems as follows.

Janatyan et al. (2018) designed a new multi-objective model for a sustainable medical distribution network based on the main concepts of sustainability effects. Minimizing the total costs and the adverse environmental impacts along with maximizing the welfare of society lead to sustainable decisions. To solve the model, NSGA-II is applied according to the three-objective function. A case study to test the model with real data is considered and the outcomes of the case study are shown the technical and strategic decisions in the pharmaceutical company. Bouziyane et al. (2020) introduced the disrupted vehicle routing problem with soft time window. In addition, medical distributors respond to maximized demands for commodities to ensure efficient and timely delivery to dynamic demands is considered. An improved multi-objective local search is developed and large neighborhood search and variable neighborhood search according to a hybrid method in the optimization of vehicle routes are used. Goodarzian et al. (2020a) developed a new MSCN model considering sustainability concepts. They formulated MILP model production-distribution problem. Then, to solve their model, meta-heuristic algorithms called genetic algorithm and particle swarm optimization algorithm are used and a hybrid algorithm is developed. Goodarzian et al. (2020b) proposed a new pharmaceutical supply chain network under uncertainty. They formulated an MINLP model for production, location, routing, and distribution problems. Their main aims were to minimize the total costs and delivery time of the medicine products and to maximize reliability. They developed a new approach called a fuzzy-robust programming to tackle with uncertain parameters. Thus, meta-heuristic algorithms are used to solve their model. Janatyan et al. (2021) designed a sustainable medicine distribution network under uncertainty with multi-objective MILP model. To tackle with uncertain parameters, robust approach was used. To solve their model, NSGA-II and multi-objective PSO algorithms are employed. Goodarzian et al. (2021a) proposed an integrated sustainable MSCN for production, distribution, inventory, allocation, location problems. They designed a multi-objective, multi-level, multi-product, and multi-period MILP model considering perishability of medicines for MSCN. They developed three hybrid meta-heuristic algorithms, namely, ant colony optimization, fish swarm algorithm, and firefly algorithm, hybridized with variable neighborhood search to solve their model. They suggested a real case study in Iran. Sazvar, Zokaee, Tavakkoli-Moghaddam et al. (2021) developed a sustainable MSCN under uncertainty. They provided a scenario-based MILP model for designing a sustainable MSCN. Hence, they developed a hybrid solution method by combining the LP-metrics approach with a heuristic algorithm. Finally, a real case study was investigated to assess the application of their model. Ahmadini et al. (2021) presented a multi-objective optimization modeling of the sustainable green supply chain network. They formulated a multi-item multi-objective MILP model for inventory and production management. To solve their model, fuzzy goal programming was used. Goodarzian et al. (2021b) designed an MSCN for location, production, distribution, transportation, inventory holding problems. They formulated a multi-echelon multi-product multi-period bi-objective MILP model under production technology policy. Their main aims were to minimize the total costs of the network and the total time the transportation. To solve their model, meta-heuristic algorithms, namely, Improved Ant Colony Optimization (IACO) and Improved Harmony Search (IHS) algorithms were developed. Finally, they used numerical examples to validate their proposed model. The summaries of the literature review are reported in Table 1.

Furthermore, the summarization of the most relevant recent general discussions is explained. (see Meiler, Tonke, Grunow, & Günther, 2015; Narayana, Pati, & Vrat, 2014; Rossetti, Handfield, & Dooley, 2011; Settanni, Harrington, & Srai, 2017; Shah, 2004; Tsao & Lu, 2012; Vosooghidizaji, Taghipour, & Canel-Depitre, 2020; Sbai and Berrado, 2018) that are the related to the MSCNs. Then, the examined papers display that supply chain network research remains far from sufficient to investigate the industry of GMSCN challenges. Besides, none of the above-mentioned research works did not consider environmental impacts and multi-modal transportation related to the integrated allocation-location-production-distribution-routing-inventory holding-purchasing problem in the GMSCN model under uncertainty simultaneously. More importantly, the design of a GMSCN due to the integration of allocation, location, production, distribution, routing, inventory holding, and purchasing problems considering environmental impacts have not been paid enough attention before. In this regard, the first novelty of this paper, multi-modal transportation is considered for the first time. Secondly, some examined papers in the literature review considered CO2 emission, but this paper states the environmental impacts related to the establishment of pharmacies, hospitals and focusing on greenhouse gases such as released carbon dioxide by vehicles simultaneously for the first time. Then, the main aims of the GMSCN is to minimize total costs, including inventory holding, production, transportation, packing, purchasing, penalty, tariff costs, and fixed costs and environmental aspects. Another contribution of the current paper compared to similar papers is relevant to the parameters of the purchasing, penalty, and tariff costs and also the parameters related to the environmental effects (establishing pharmacies and hospitals and the released CO2 emission) that are considered for the first time simultaneously. To address the available gaps in this work, a bi-objective, multi-period multi-product MILP model for the GMSCN problem along with a multi-modal transportation is developed. To cope with uncertain parameters, fuzzy programming is employed that the considered uncertain parameters in transportation and inventory holding costs. In terms of the solution methodology, one of the important novelties relates to solution methodology in this paper. To solve the proposed model, SEO, IKH, ISSO, and HWO-SA algorithms are utilized. Additionally, two novel hybrid meta-heuristic algorithms, namely, HFFA-SA and HSEO-FFA are developed to find Pareto optimal solutions and to solve the GMSCN problem in large-scale problems, which are not used in the reviewed papers related to these algorithms. The results of both proposed hybrid metaheuristic algorithms are compared with those obtained with other suggested metaheuristic algorithms. The HSEO-FFA algorithm is one of the newest evolutionary algorithms, which has robust efficiency and performance than other proposed algorithms. Therefore, the main advantage of improved global search in the form of an HSEO-FFA with a local search is the improvement in the convergence speed to Pareto optimal and near-optimal solutions. The proposed solution drastically improves the basic structure of SEO and FFA algorithms considering HSEO-FFA to decrease the computational time. Moreover, the results indicate the HSEO-FFA algorithm has more robust than other proposed metaheuristic algorithms.

The main contributions of this work, which differentiates our paper from the existing literature are listed as follows:

Table 1
The summaries of the literature review.

References	The type of the model	The type of the uncertainty	Objective	The type of problem							Multi-modal transportation	Pharmacies/ hospitals Establishing	CO_2 emission	Solution methodology
				Production	Allocation	Location	Routing	Distribution	Inventory	Purchasing				
Sousa et al. (2005)	MILP		Minimizing total costs		*			*						Lagrangian relaxation
Susarla and Karimi (2012)	MILP		Minimizing total costs	*				*						Exact methods
Mousazadeh et al. (2015)	MILP	robust possibilistic	Minimizing total costs and unfulfilled demands		*	*		*						Exact methods
Hansen and Grunow (2015)	MILP	Stochastic	Minimizing total costs					*						Exact methods
Weraikat et al. (2016)	ILP		Minimizing total costs		*			*						Exact methods
El Mokrini et al. (2016)	MILP		Minimizing total costs	*										PROMETHEE and fuzzy AHP methods
Nematollahi et al. (2017)	MILP	Stochastic	Minimizing economic effects and Maximizing social effects		*	*								Exact methods
Zahiri et al. (2017)	MILP	fuzzy stochastic-possibilistic	Minimizing total costs and unfulfilled demands					*						Heuristic methods
Mehralian et al. (2017)	MILP		Recognize and prioritize factors affecting the coordination of a PSC	*										AHP method
Janatyan et al. (2018)	MILP		Minimizing the total costs and the adverse environmental impacts along with maximizing the welfare of society					*					*	NSGA-II
Bijaghini and SeyedHosseini (2018)	MILP	Robust	Minimization of the budget during the scheduled time and the shortage amount associated with the lost sale	*			*		*					Benders decomposition
Zahiri et al. (2018)	MILP	Robust-possibilistic	Minimizing total costs and unmet demands	*			*	*						CPLEX
Vishwakarma et al. (2019)	MILP		Prioritizing rank barriers in the medical industry											Fuzzy AHP
Roshan et al. (2019)	MILP		Minimizing total costs and unmet demands, maximizing of the satisfaction of social responsibility					*						Branch & bound
Weraikat et al. (2019)	MINLP		Minimizing of the quantity of the expired medicines						*					
Singh and Goh (2019)	MILP	Fuzzy	Minimizing total costs and maximizing total value of purchase						*					Branch & bound
Priyan and Mala (2020)	MILP		Minimizing total costs and unmet demands							*				Game theory
Bouchra et al. (2020)	MILP		Minimizing total costs				*	*						VNS
GoodGoodarzian et al. (2020a)	MILP		Minimizing economic and environmental effects and maximizing social aspects	*				*					*	Genetic algorithm, PSO, Hybrid GA-PSO
Zandkarimkhani et al. (2020)	MILP	chance-constrained and programming	Minimizing the total costs and lost demand amount			*	*		*					Exact methods
Goodarzian et al. (2020b)	MILP	Fuzzy-robust	Minimizing total costs and delivery time, Maximizing reliability	*		*	*		*					SEO, Keshtel, SA, FFA
	MILP	Robust						*					*	NSGA-II, MOPSO

(*continued on next page*)

Table 1 (*continued*)

References	The type of the model	The type of the uncertainty	Objective	The type of problem							Multi-modal transportation	Pharmacies/ hospitals Establishing	CO_2 emission	Solution methodology
				Production	Allocation	Location	Routing	Distribution	Inventory	Purchasing				
Janatyan et al. (2021)			Minimizing economic and environmental effects and maximizing social aspects											
Goodarzian et al. (2021a)	MILP		Minimizing economic and environmental effects and maximizing social aspects	*	*	*		*	*				*	HACO-VNS, HFSA-VNS, HFA-VNC
Sazvar et al. (2021)	MILP		Minimizing economic and environmental effects and maximizing social aspects	*				*					*	LP-metric, Heuristic method
Ahmadini et al. (2021)	MILP		Minimizing economic and environmental effects and maximizing social aspects	*					*					Fuzzy goal programming
Goodarzian et al. (2021b)	MILP		Minimizing the total costs of the network and the total time the transportation	*		*		*	*				*	IHS, IACO, MOSA, MOACO, MOVNS, MOHS, CPLEX
This paper	MILP	Fuzzy	Minimizing total costs and environmental effects	*	*	*	*	*	*	*	*	*	*	SEO, IKH, ISSO, HWO-SA, HFFA-SA, HSEO-FFA

- Designing a novel multi-period, three-echelon, and multi-product GMSCN under uncertainty;
- Formulating a new bi-objective MILP model for GMSCN problem based on the multi-modal transportation for the first time;
- Integrating production, allocation, location, routing, inventory holding, purchasing, and distribution problems in the current model simultaneously for the first time;
- Considering simultaneously for the first time the environmental impacts related to the establishment of pharmacies and hospitals and produced greenhouse gas emissions, such as CO2 emission of the transportation systems;
- Developing two novel hybrid meta-heuristic algorithms called HSEO-FFA and HFFA-SA algorithms to solve the proposed model in different size problems.

4. Problem description

As it is mentioned, this study develops a new three-echelon GMSCN. Components of this network, namely, Production Centers (PCs), Distribution Centers (DCs), and customers that are pharmacies and hospitals, are considered. In general, a new multi-period, multi-product, and multi-echelon GMSCN are shown in Fig. 1. In this network, PCs are divided into two categories include Foreign Production Center (FPC) and Internal Production Center (IPC). Hence, an FPC is provided because of the medical product shortage in the IPC. Furthermore, medical products from DCs to customers (pharmacies and hospitals) and from IPC and FPC to the DCs are transferred with the multi-modal transportation system as an aerial or terrestrial (i.e., a plane, a truck, *etc.*) according to the demands of medical products and specified routes between network at different times. In this problem, several pharmacies and hospitals with opening costs and their available capacity are considered. Only one type of vehicle is eligible to be used along each route. The proposed model innovation is to consider a penalty for the extra distance traveled for each route. Also, other contributions of the proposed model related to environmental effects with the amount of carbon dioxide released. Besides, according to the greenness of the model, the effect related to the opening of environmental facilities for pharmacy and hospital are (θ_p) and (θ_h) respectively. In order to control the transportation costs, the parameters for maximum desired distance (π_v) and the penalty coefficient in the objective function (μ) are considered. The assumptions of this problem are explained as follows:

- o Each vehicle can traverse a maximum of one route per period;
- o There is no direct route from FPCs to pharmacies, hospitals, DCs;
- o Medical products are transferred through the air transportation system if the available airport at those levels of the network, otherwise it will be transmitted through the land transportation system. Additionally, the transportation of medical products from FPCs will only be possible through the air transportation system;
- o In the case of transportation cost control, the penalty function is considered to be predefined for an undesirable cost amount as well as each unit faces the ruin of medical products must pay the penalty cost in each period;
- o There are many pharmacies and hospitals that need to be decided about the establishment of potential locations;
- o The environmental impacts related to the establishment of pharmacies and hospitals are considered;
- o The amount of releasing carbon dioxide (CO_2) by vehicles is considered.

4.1. Notations

	Sets
i	Set of IPC$i \in \{1,2,\cdots,I\}$
f	Set of FPC $f \in \{1,2,\cdots,F\}$
m	Set of medical products$m \in \{1,2,\cdots,M\}$
p	Set of customers (pharmacies)$p \in \{1,2,\cdots,P\}$
h	Set of customers (hospitals)$h \in \{1,2,\cdots,H\}$
d	Set of DC$d \in \{1,2,\cdots,D\}$
v	Set of vehicles (airplane)$v \in \{1,2,\cdots,V\}$
k	Set of vehicles (Nissan and pickup truck)$k \in \{1,2,\cdots,K\}$
r	Set of routes$r \in \{1,2,\cdots,R\}$
t	Set of time period$t \in \{1,2,\cdots,T\}$
	Parameters
$\widetilde{C}^t_{im}$	The cost of inventory holding at IPC i for medical product m at the period t
$\widetilde{C}^t_{fm}$	The cost of inventory holding at FPC f for medical product m at the period t
$\widetilde{C}^t_{dm}$	The cost of inventory holding at DC d for medical product m at the period t
IL^t_{dm}	Inventory level at DC d for medical product m at the period t
β_p	Fixed cost for the establishment of pharmacy$p$
β_h	Fixed cost for the establishment of hospital$h$
P^t_m	The cost of penalty for the perished medical product m at the period t
P^t_{mi}	The cost of production to produce medical product m at the IPC i at the period t
P^t_{mf}	The cost of production to produce medical product m at FPC f at the period t
$\widetilde{T}^t_{midv}$	Transportation cost for medical product m from IPC i to DC d by vehicle v at the period t
$\widetilde{T}^t_{midk}$	Transportation cost for medical product m from IPC i to DC d by vehicle k at the period t
$\widetilde{T}^t_{mfiv}$	Transportation cost for medical product m from FPC f to IPC i by vehicle v at the period t
$\widetilde{T}^t_{mdpv}$	Transportation cost for medical product m from DC d to pharmacy p by vehicle v at the period t
$\widetilde{T}^t_{mdpk}$	Transportation cost for medical product m from DC d to pharmacy p by vehicle k at the period t
$\widetilde{T}^t_{mdhv}$	Transportation cost for medical product m from DC d to hospital h by vehicle v at the period t
$\widetilde{T}^t_{mdhk}$	Transportation cost for medical product m from DC d to hospital h by vehicle k at the period t
$\widetilde{T}^t_{mphk}$	Transportation cost for medical product m from pharmacy p to hospital h by vehicle k at the period t
L^t_m	The cost of tariff of medical product m at the period t in the airport
EP^t_{md}	Packing cost of medical product m in DC d at the period t
S^t_{mdi}	Purchase cost of medical product m by DC d from the IPC i at the period t
S^t_{mif}	Purchase cost of medical product m by IPC i from the FPC f at the period t
S^t_{mpd}	Purchase cost of medical product m by pharmacy p from the DC d at the period t
S^t_{mhd}	Purchase cost of medical product m by hospital h from the DC d at the period t
S^t_{mph}	Purchase cost of medical product m by pharmacy p from the hospital h at the period t
σ_{vk}	The amount of released carbon dioxide (CO_2) by the vehicles v and k per unit of distance
d_{id}	Distance between IPC i and DC d
d_{fi}	Distance between FPC f and IPCi
d_{dp}	Distance between DC d and pharmacy p
d_{dh}	Distance between DC d and hospital h
d_{ph}	Distance between pharmacy p hospital h
δ_{dpm}	Intact rate from DC d to pharmacy p for medical product$m$
δ_{dhm}	The rate of intact from DC d to hospital h for medical product$m$
π_v	The maximum distance traveled by the transportation system v between pharmacy and hospital, which is determined by the policy adopted by the IPCs and FPCs.
ϕ_d	The capacity of DC d
ϕ_v	The capacity of vehicle v
ϕ_k	The capacity of vehicle$k$
ϕ_p	The capacity of pharmacy$p$
ϕ_h	The capacity of hospital$h$
K^t_{mdi}	Medical product m demand required by DC d from the IPC i at the period t

(continued on next column)

(continued)

	Sets
K^t_{mif}	Medical product m demand required by IPC i from the FPC f at the period t
K^t_{mpd}	Medical product m demand required by pharmacy p from the DC d at the period t
K^t_{mhd}	Medical product m demand required by hospital h from the DC d at the period t
K^t_{mph}	Medical product m demand required by pharmacy p from the hospital h at the period t
I^t_{md}	Medical product amount m storage in the DC d as inventory at the period t
θ_p	The environmental impacts for the establishment of pharmacy$p$
θ_h	The environmental impacts for the establishment of hospital$h$
J^t_{md}	Incipient inventory of medical product m in the DC d at the period t
MAX	Maximum the number of facilities establishing for pharmacies and hospitals
Big M	A big number
μ	The number of considered penalty for the extra distance traveled between levels in the proposed network
	Decision variables
Q^t_{mi}	The amount of inventory of medical product m in the IPC i at the period t
Q^t_{mf}	The amount of inventory of medical product m in the FPC f at the period t
Q^t_{md}	The amount of inventory of medical product m in the DC d at the period t
W^t_{mp}	The perished amount of the medical product$m$ at the pharmacy p at the end of the period t
W^t_{mh}	The perished amount of the medical product m at the hospital h at the end of the period t
X^t_{mi}	The amount of production of the medical product m at the IPC i at the period t
X^t_{mf}	The amount of production of the medical product m at the FPC f at the period t
N^{tr}_{midv}	The amount of the medical product m transported from IPC i to DC d by vehicle v on route r at the period t
N^{tr}_{midk}	The amount of the medical product m transported m from IPC i to DC d by vehicle k on route r at the period t
N^{tr}_{mfiv}	The amount of the medical product m transported from FPC f to IPC i by vehicle v on route r at the period t
N^{tr}_{mdpv}	The amount of the medical product m transported m from DC d to pharmacy p by vehicle v on route r at the period t
N^{tr}_{mdpk}	The amount of the medical product m transported from DC d to pharmacy p by vehicle k on route r at the period t
N^{tr}_{mdhv}	The amount of the medical product m transported from DC d to hospital h by vehicle v on route r at the period t
N^{tr}_{mdhk}	The amount of the medical product m transported from DC d to hospital h by vehicle k on route r at the period t
N^{tr}_{mphk}	The amount of the medical product m transported from pharmacy p to hospital h by vehicle k on route r at the period t
Z^t_{mdi}	The quantity of purchasing of medical product m by DC d from IPC i at the period t
Z^t_{mif}	The quantity of purchasing of medical product m by IPC i from FPC f at the period t
Z^t_{mpd}	The quantity of purchasing of medical product m by pharmacy p from DC d at the period t
Z^t_{mhd}	The quantity of purchasing of medical product m by hospital h from DC d at the period t
Z^t_{mph}	The quantity of purchasing of medical product m by pharmacy p from hospital h at the period t
A^t_{md}	The excess demand quantity for medical product m by DC d at the period t
B^t_{md}	The excess supply quantity for medical product m by DC d at the period t
λ_p	If pharmacy p is established equal 1; otherwise 0
λ_h	If hospital h is established equal 1; otherwise 0
g^t_v	If transportation system v travels from a echelon to other echelon in network at the period t equal 1; otherwise 0
g^t_k	If transportation system k travels from a echelon to other echelon in network at the period t equal 1; otherwise 0
O_{mdt}	The packed amount of the medical product m in DC d at the period t
G^{tr}_{id}	If IPC i is allocated to DC d on route r at the period t equal 1; otherwise 0
G^{tr}_{fi}	If FPC f is allocated to IPC i on route r at the period t equal 1; otherwise 0
η_{phv}	If the medical products are transported from the pharmacy p to the hospital h using the vehicle v equal 1; otherwise 0
ψ_{phv}	The amount of extra distance traveled from the pharmacy p to the hospital h using vehicle$v$

(continued on next page)

(*continued*)

	Sets
Y_{dp}^{tr}	If DC d is allocated to pharmacy p on route r at the period t equal 1; otherwise 0
Y_{dh}^{tr}	If DC d is allocated to hospital h on route r at the period t equal 1; otherwise 0

4.2. Green medicine supply chain network mathematical model

$$
\begin{aligned}
Min\, F_1 = &\{\sum_i\sum_m\sum_t\left(\widetilde{C}^t_{im}\times Q^t_{mi}\right)+\sum_f\sum_m\sum_t\left(\widetilde{C}^t_{fm}\times Q^t_{fm}\right)+\sum_d\sum_m\sum_t\left(\widetilde{C}^t_{dm}\times Q^t_{md}\right)\Big\}+\\
&\{\sum_m\sum_t P^t_m\left(\sum_p W^t_{mp}+\sum_h W^t_{mh}\right)\Big\}+\{\sum_m\sum_t(L^t_m\times(\sum_r\sum_v(\sum_i\sum_d N^{tr}_{midv}+\sum_f\sum_i N^{tr}_{fidv}+\sum_d\sum_p N^{tr}_{mdpv}+\sum_d\sum_h N^{tr}_{mhpv})\}+\\
&\{\sum_m\sum_i\sum_t(P^t_{mi}\times X^t_{mi})+\sum_m\sum_f\sum_t(P^t_{mf}\times X^t_{mf})\}+\\
&\{\sum_i\sum_d d_{id}\left(\sum_m\sum_v(\widetilde{T}^t_{midv}\times\sum_t N^{tr}_{midv})+\sum_m\sum_k(\widetilde{T}^t_{midk}\times\sum_t N^{tr}_{midk})\right)+\\
&\sum_f\sum_i d_{fi}\left(\sum_m\sum_v(\widetilde{T}^t_{fmiv}\times\sum_t N^{tr}_{mfiv})\right)+\sum_d\sum_p d_{dp}\left(\sum_m\sum_v(\widetilde{T}^t_{mdpv}\times\sum_t N^{tr}_{mdpv})+\sum_m\sum_k(\widetilde{T}^t_{mdpk}\times\sum_t N^{tr}_{mdpk})\right)\}+\\
&\sum_d\sum_h d_{dh}\left(\sum_m\sum_v(\widetilde{T}^t_{mdhv}\times\sum_t N^{tr}_{mdhv})+\sum_m\sum_k(\widetilde{T}^t_{mdhk}\times\sum_t N^{tr}_{mdhk})\right)+\sum_p\sum_h d_{ph}\left(\sum_m\sum_k(\widetilde{T}^t_{mphk}\times\sum_t N^{tr}_{mphk})\right)\}\\
&\{\sum_d\sum_t\sum_m(O_{mdt}\times EP^t_{md})\}+\{\sum_p(\beta_p\times\lambda_p)+\sum_h(\beta_h\times\lambda_h)\}+\\
&\{\sum_m\sum_d\sum_i\sum_t(S^t_{mdi}\times Z^t_{mdi})+\sum_m\sum_i\sum_f\sum_t(S^t_{mif}\times Z^t_{mif})+\sum_m\sum_p\sum_d\sum_t(S^t_{mpd}\times Z^t_{mpd})+\\
&\sum_m\sum_h\sum_d\sum_t(S^t_{mhd}\times Z^t_{mhd})+\sum_m\sum_p\sum_h\sum_t(S^t_{mph}\times Z^t_{mph})\}+\{\sum_p\sum_h\sum_v\left(\psi_{phv}\times\widetilde{T}_v\times\mu\right)\Big\}
\end{aligned}
\tag{1}
$$

The objective function (1) is defined to decrease the total cost in the GMSCN including penalty, tariff, transportation, production, inventory holding, packaging, established fixed cost, purchasing costs, penalty costs related to extra mileage. In the first bracket, inventory holding costs are considered at the levels of the IPC, FPC, and DC for medical products. In the second bracket, the penalty cost of perished medical products is considered. In the third bracket, a tariff cost for the aerial transporting of medical products between the levels of the network and transported to the airport tariff office is provided. In the fourth bracket, the production costs related to the medical products in the IPCs and FPCs. In the fifth bracket, the transportation costs relevant to the medical products at different times and using different transportation systems between various routes in the proposed network are considered as a variable parameter. Then, the packaging and preparation cost of medical products in the DCs are designated in the sixth bracket. The fixed costs related to the opening of IPCs, FPCs, pharmacies, and hospitals term in the seventh bracket. In the eighth bracket, the purchase costs of medical products by DCs from IPCs and FPCs and by customers from DCs are inserted. Finally, the penalty cost is calculated for the extra traveled distance in the proposed model.

$$Min\, F_2=\sum_p(\theta_p\lambda_p)+\sum_h(\theta_h\lambda_h)+\sum_p\sum_h\sum_v(d_{hp}\eta_{phv}\sigma_{vk}) \tag{2}$$

Another contribution of this paper relates to the second objective. Environmental effects of the whole GMSCN is considered in the objective function (2). In this equation, the first and second terms denote the environmental impacts related to the establishment of pharmacies and hospitals. In the third term, the green effect relates to the used vehicles until the rate of released carbon dioxide (CO_2) by vehicles is calculated.

$$\sum_i\sum_d K^t_{mid}+\sum_i\sum_f K^t_{mif}+\sum_d\sum_p K^t_{mdp}+\sum_d\sum_h K^t_{mdh})\times g^t_v\leqslant\phi_v \quad \forall m\in M, t\in T, v\in V \tag{3}$$

$$(\sum_i\sum_d K^t_{mid}+\sum_i\sum_f K^t_{mif}+\sum_d\sum_p K^t_{mdp}+\sum_d\sum_h K^t_{mdh})\times g^t_k\leqslant\phi_k \quad \forall m\in M, t\in T, k\in K \tag{4}$$

$$\sum_p\sum_r Y^{tr}_{dp}\leqslant 1 \qquad \forall d\in D, \forall t\in T \tag{5}$$

$$\sum_h\sum_r Y^{tr}_{dh}\leqslant 1 \qquad \forall d\in D, \forall t\in T \tag{6}$$

$$\sum_d((\sum_r Y^{tr}_{dp}\times\delta_{dpm}+A^t_{md}-B^t_{md})=K^t_{mdp}) \quad \forall t\in T, m\in M, p\in P \tag{7}$$

$$\sum_d((\sum_r Y^{tr}_{dh}\times\delta_{dhm}+A^t_{md}-B^t_{md})=K^t_{mdh}) \quad \forall h\in H, \forall t\in T, \forall m\in M \tag{8}$$

$$I^t_{md-1}=\sum_m\sum_p K^t_{mpd}+\sum_m\sum_h K^t_{mhd}+I^t_{md} \quad \forall d\in D, \forall t\in T \tag{9}$$

$$\sum_t IL^t_{md}=J_{md} \quad \forall d\in D, \forall m\in M \tag{10}$$

$$\sum_m\sum_i\sum_d\sum_t\sum_r N^{tr}_{midv}\leqslant\phi_v \qquad \forall v\in V \tag{11}$$

$$\sum_m\sum_i\sum_d\sum_t\sum_r N^{tr}_{midk}\leqslant\phi_k \qquad \forall k\in K \tag{12}$$

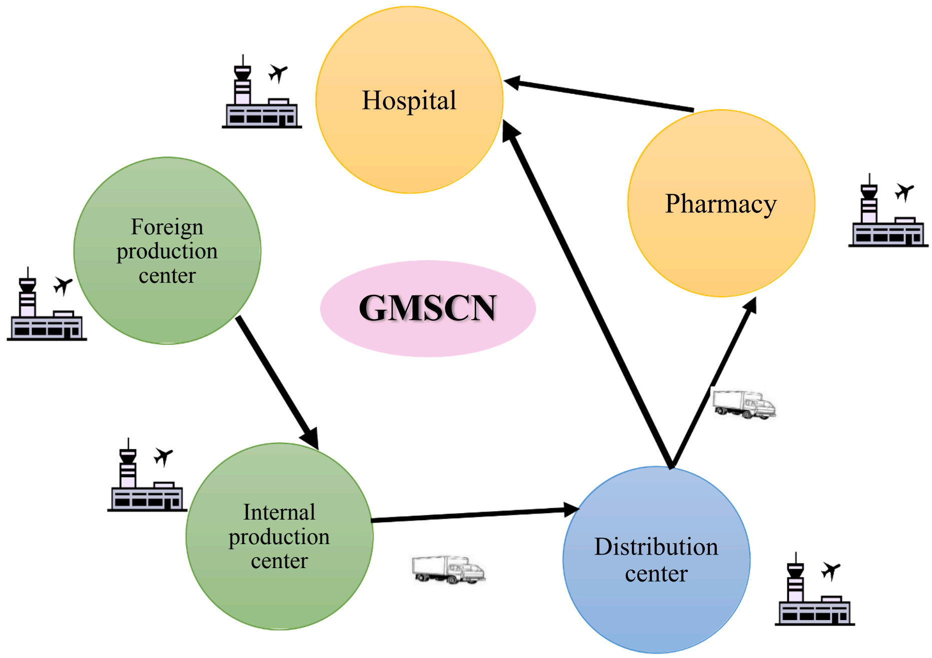

Fig. 1. The structure of three-echelon GMSCN.

$$\sum_m\sum_f\sum_i\sum_t\sum_r N^{tr}_{mfiv} \leqslant \phi_v \qquad \forall v \in V \tag{13}$$

$$\sum_m\sum_d\sum_p\sum_t\sum_r N^{tr}_{mdpv} \leqslant \phi_v \qquad \forall v \in V \tag{14}$$

$$\sum_m\sum_d\sum_p\sum_t\sum_r N^{tr}_{mdpk} \leqslant \phi_k \qquad \forall k \in K \tag{15}$$

$$\sum_m\sum_d\sum_h\sum_t\sum_r N^{tr}_{mdhv} \leqslant \phi_v \qquad \forall v \in V \tag{16}$$

$$\sum_m\sum_d\sum_h\sum_t\sum_r N^{tr}_{mdhk} \leqslant \phi_k \qquad \forall k \in K \tag{17}$$

$$\sum_m\sum_p\sum_h\sum_t\sum_r N^{tr}_{mphk} \leqslant \phi_k \qquad \forall k \in K \tag{18}$$

$$(g^t_v + g^t_k) - Y^{tr}_{dp} \leqslant 1 \qquad \forall d \in D, \forall p \in P, v \in V, k \in K, \forall r \in R, \forall t \in T \tag{19}$$

$$(g^t_v + g^t_k) - Y^{tr}_{dh} \leqslant 1 \qquad \forall d \in D, \forall h \in H, v \in V, k \in K, \forall r \in R, \forall t \in T \tag{20}$$

$$\sum_r G^{tr}_{id} \leqslant 1 \qquad \forall d \in D, \forall i \in I, \forall t \in T \tag{21}$$

$$\sum_r G^{tr}_{fi} \leqslant 1 \qquad \forall f \in F, \forall i \in I, \forall t \in T \tag{22}$$

$$\sum_r Y^{tr}_{dp} \leqslant 1 \qquad \forall d \in D, \forall p \in P, \forall t \in T \tag{23}$$

$$\sum_r Y^{tr}_{dh} \leqslant 1 \qquad \forall h \in H, \forall d \in D, \forall t \in T \tag{24}$$

$$\sum_p \lambda_p = MAX \tag{25}$$

$$\sum_h \lambda_h = MAX \tag{26}$$

$$\sum_d\sum_r\sum_t Y^{rt}_{dp} \leqslant \lambda_p \times BigM \quad \forall p \in P \tag{27}$$

$$\sum_d\sum_r\sum_t Y^{rt}_{dh} \leqslant \lambda_h \times BigM \quad \forall h \in H \tag{28}$$

$$\sum_d\sum_r\sum_t Y^{rt}_{dp} = 1 \quad \forall p \in P \tag{29}$$

$$\sum_d\sum_r\sum_t Y^{rt}_{dh} = 1 \quad \forall h \in H \tag{30}$$

$$\psi_{phv} \geqslant \left(d_{ph} \times \eta_{phv}\right) - \pi_v \qquad \forall p \in P, \forall h \in H, \forall v \in V \tag{31}$$

$$\psi_{phv} \geqslant 0 \qquad \forall p \in P, \forall h \in H, \forall v \in V \tag{32}$$

$$\left(\sum_r N^{tr}_{mdpv} + \sum_r N^{tr}_{mdhv}\right) \leqslant bigM\left(\sum_r Y^{tr}_{dp} + \sum_r Y^{tr}_{dh}\right) \qquad \forall m \in M, \forall p \in P, \forall h \in H, \forall d \in D, \forall t \in T \tag{33}$$

$$\sum_d Z^t_{mdi} + Q^{t-1}_{mi} - Q^t_{mi} = X^t_{mi} \qquad \forall m \in M,\ i \in I,\ t \in T \tag{34}$$

$$\sum_f Z^t_{mif} + Q^{t-1}_{mf} - Q^t_{mf} = X^t_{mf} \qquad \forall m \in M,\ i \in I,\ t \in T \tag{35}$$

$$\sum_m\sum_p\sum_t Z^t_{mpd} \leqslant \phi_d \quad \forall d \in D \tag{36}$$

$$\sum_m\sum_h\sum_t Z^t_{mhd} \leqslant \phi_d \quad \forall d \in D \tag{37}$$

$$\sum_m\sum_p\sum_t Z^t_{mph} \leqslant \phi_h \quad \forall h \in H \tag{38}$$

$$Q_{mf}^{t-1}+(\sum_r\sum_i(\sum_v N_{mfiv}^{tr})+(\sum_k N_{mfik}^{tr}))=Q_{mf}^{t}+K_{mif}^{t}\quad \forall m\in M,f\in F,\ t\in T \tag{39}$$

$$Q_{mi}^{t-1}+(\sum_r\sum_d(\sum_v N_{midv}^{tr})+(\sum_k N_{midk}^{tr}))=Q_{mi}^{t}+K_{mdi}^{t}\quad \forall m\in M,\ i\in I,\ t\in T \tag{40}$$

$$Q_{md}^{t-1}+\left(\sum_r\sum_i\left(\sum_v N_{midv}^{tr}\right)+\left(\sum_k N_{midk}^{tr}\right)\right)=Q_{md}^{t}+K_{mdi}^{t}\ \forall m\in M,\ d\in D,\ t\in T \tag{41}$$

constraint (33), at least a DC must be allocated to customers (pharmacies and hospitals), if a vehicle v travels from a DCs to pharmacies and hospitals. Constraints (34) and (35) joint the purchasing and production decisions together, through the inventory balance of medical products in IPC and FPC respectively. These constraints illustrate that the transportation of medical products, which is equal to the purchased medical products in period t plus the amount of the inventory in the previous period minus the amount of the inventory in period t should be equal to the amount of producing medical products. Constraints (36)-(38) describe the purchasing limitations of medical products as a function of t so that these can cover the demand daily. Then, the inventory balance limitations of medical products at IPC, FPC, DC are shown respectively in constraints (39)-(41). Eventually, constraints (42) and (43) depict the type of the variables of decision.

$$Q_{mi}^{t},\ Q_{mf}^{t},\ Q_{md}^{t},\ IL_{md}^{t},\ W_{mp}^{t},\ W_{mh}^{t},\ U_{mk},\ X_{mi}^{t},\ X_{mf}^{t},\ N_{midv}^{tr},\ N_{mfiv}^{tr},\ N_{mdpv}^{tr},\ N_{mdpk}^{tr},\ N_{mdhv}^{tr},\ N_{mdhk}^{tr},\ N_{mphk}^{tr},\ Z_{mdi}^{t},\ Z_{mif}^{t},\ Z_{mpd}^{t},\ Z_{mhd}^{t},\ Z_{mph}^{t},\ A_{md}^{t},\ B_{md}^{t},\ O_{mdt},\ \psi_{phv},\ \geqslant 0 \tag{42}$$

$$g_v^t, g_k^t, G_{id}^{tr}, G_{fi}^{tr}, Y_{dp}^{tr}, Y_{dh}^{tr}, \eta_{phv}, \lambda_p, \lambda_h \in \{0,1\} \tag{43}$$

Constraints (3) and (4) are related to the capacity of the transportation systems in each period, which should be left equations less than the vehicle capacities v and k, respectively. In the constraints (5) and (6), only a DC is devoted to the customer (pharmacy and hospital). In other words, both binary variables, namely, Y_{dp}^{tr} and Y_{dh}^{tr} must be lower than 1 at each period on different routes or only one DC is assigned to the pharmacy and hospital. K_{mpd}^{t} and K_{mhd}^{t} indicate required medical product demands by pharmacy and hospital from DC at each period, which should be equal to $\sum_d(\sum_r Y_{mdp}^{tr}\times\delta_{dpm}+A_{md}^{t}-B_{md}^{t})$ and $\sum_d(\sum_r Y_{mdh}^{tr}\times\delta_{dhm}+A_{p'd}^{t}-B_{md}^{t})$ respectively which are related to the balance of the DCs in the constraints (7) and (8). In constraint (9), The summation of required medical product demand by the pharmacy ($\sum_m\sum_p K_{mpd}^{t}$) and by the hospital($\sum_m\sum_h K_{mhd}^{t}$) form the DC and the amount of medical product stored at the DC as inventory (I_{md}^{t}) at each period, which should be equal to the amount of medical product stored at the DC as inventory (I_{md-1}^{t}) at the previous period. In other words, this equation displays inventory balance in DC. $IL_{md1}=J_{md}$ that is associated with the balance of initial inventory in DC. The IL_{md1} shows the amount of inventory of medical products in DC during the first period and J_{md} initial inventory of medical products in DC in constraint (10). Constraints (11) -(18) compel that the capacity of different vehicles should be observed. Constraints (19) and (20) illustrate the routes of each transportation system in a sequence, respectively. Constraints (21) - (24) show the only one route between each IPC and DC, each FPC and DC, and each DC, pharmacy and hospital or in other words $\sum_r Y_{dp}^{tr}$, $\sum_r Y_{dh}^{tr}$, $\sum_r G_{id}^{tr}$ and $\sum_r G_{fi}^{tr}$ must be less than 1. Constraints (25) and (26) indicate the maximum required number for the opening of the pharmacy and hospital. Constraints (27) and (28) guarantee that if and only if the pharmacy and hospital are opened, those can be assigned to a DC. Each pharmacy and hospital should only be assigned to a DC or $\sum_d\sum_r\sum_t Y_{dp}^{rt}$ and $\sum_d\sum_r\sum_t Y_{dh}^{rt}$ should be equal to 1 which is indicated by constraints (29) and (30). Constraints (31) and (32) confirm the distance traveled by the vehicle must not exceed a desirable value. Otherwise, it is calculated by the penalty coefficient in the objective function. In terms of

4.3. Fuzzy programming approach

Hence, the literature has examined several fuzzy, robust, stochastic programming, etc., which were used to convert the uncertain to deterministic model. Among them, Fuzzy is a well-known technique and easy to implement (Zimmermann, 1978). This advantage motivates us to utilize it again in our paper. There are several applications for this technique, including the job shop scheduling problem (Sakawa & Kubota, 2000), the green closed-loop supply chain network problem (Fakhrzad & Goodarzian, 2019), the pharmaceutical supply chain problem (Singh & Goh, 2019), production–distribution network problem (Goodarzian & Hosseini-Nasab, 2019), the home health care problem (Goodarzian et al., 2021c), the textile supply chain management (Tayyab & Sarkar, 2021), etc.

As indicated in Fig. 2, triangular fuzzy numbers (TFNs) are utilized to propose the inventory holding and transportation costs in this study. Triangular fuzzy numbers are also a special form of trapezoidal fuzzy numbers. In fact, in fuzzy trapezoidal numbers, there is a range that has a membership function equal to one, but in triangular numbers, there is a point that has a membership function equal to one. So when we use triangular fuzzy numbers, we are actually using a special form of trapezoidal numbers, and the main reason for this use is its easy understanding and intuitive interpretation. Therefore, we used a triangular number to get a better intuitive understanding of the problem. In addition, this type of fuzzy number is very common due to its very high computational efficiency as well as calculations with this type of number are very simple and understandable. A TFN can be specified by three parameters $F=(f^p,f^m,f^o)$ (Fakhrzad & Goodarzian, 2019). According to the computational simplicity in comparison with other fuzzy data, the triangulated data method is preferred in this study, as, it is calculated in the equation (32).

$$\begin{aligned}\widetilde{\alpha}+\widetilde{\beta}&=(\alpha_1+\beta_1,\ \alpha_2+\beta_2,\ \alpha_3+\beta_3)\\ \widetilde{\alpha}-\widetilde{\beta}&=(\alpha_1-\beta_3,\ \alpha_2-\beta_2,\ \alpha_3-\beta_1)\\ \widetilde{\alpha}\times\widetilde{\beta}&=(\alpha_1\times\beta_1,\ \alpha_2\times\beta_2,\ \alpha_3\times\beta_3)\\ \widetilde{\alpha}/\widetilde{\beta}&=(\alpha_1/\beta_3,\ \alpha_2/\beta_2,\ \alpha_3/\beta_1)\end{aligned} \tag{32}$$

Once the appropriate fuzzy spectrum has been selected and the fuzzy operations have been performed on the values, you will finally arrive at results that will normally be fuzzy. Then, these fuzzy results are not easy to understand and interpret, so they must be converted to deterministic numbers. The process of converting fuzzy numbers to deterministic numbers is called defuzzification. The equation (33) is exploited for the defuzzification of TFNs as follows:

$$Defuzzification\,(\widetilde{\alpha}) = \frac{(\alpha_1 + 2 \times \alpha_2 + \alpha_3)}{4} \tag{33}$$

In this paper, a two-stage method is used to tackle the problem. In the first process, the presented model is defuzzified by converting the main problem into an auxiliary crisp multi-objective MILP that is equal to the main problem. Hence, in the next process, a bi-process interactive fuzzy programming method is explained to attain a satisfactory compromise solution. In terms of an auxiliary crisp multi-objective MILP model, TFNs are applied to calculate the uncertainty related to the task processing times. In general, the triangular fuzzy processing time is stated by triplet points. A fuzzy triangular membership function (MF) contains three main elements involving: the value of the optimistic (f^p), the value of the possible(f^m), and the value of the pessimistic (f^o), as is shown in Fig. 2. The values of pessimistic and optimistic have the lowest degree of membership ($\mu_f(f^o) = \mu_f(f^o) = 0$). The value of the probability is assumed within the interval and has a maximum membership degree ($\mu_f(f^m) = 1$). It is supposed that all other points determined among these three points have the degree of the membership that values modify linearly between [0,1]. Furthermore, the parameters of the GMSCN model, including inventory holding and transportation costs parameters are illustrated based on the above descriptions as below:

$$\widetilde{C}^t_{im} = \left(C^{ot}_{im}, C^{mt}_{im}, C^{pt}_{im}\right)$$

$$\widetilde{C}^t_{fm} = \left(C^{ot}_{fm}, C^{mt}_{fm}, C^{pt}_{fm}\right)$$

$$\widetilde{C}^t_{dm} = \left(C^{ot}_{dm}, C^{mt}_{dm}, C^{pt}_{dm}\right)$$

$$\widetilde{T}^t_{midv} = \left(T^{ot}_{midv}, T^{mt}_{midv}, T^{pt}_{midv}\right)$$

$$\widetilde{T}^t_{midk} = \left(T^{ot}_{midk}, T^{mt}_{midk}, T^{pt}_{midk}\right)$$

$$\widetilde{T}^t_{mfdk} = \left(T^{ot}_{mfdk}, T^{mt}_{mfdk}, T^{pt}_{mfdk}\right)$$

$$\widetilde{T}^t_{mdpv} = \left(T^{ot}_{mdpv}, T^{mt}_{mdpv}, T^{pt}_{mdpv}\right)$$

$$\widetilde{T}^t_{mdpk} = \left(T^{o}c^{t}_{mdpk}, T^{mt}_{mdpk}, T^{pt}_{mdpk}\right)$$

$$\widetilde{T}^t_{mdhv} = \left(T^{ot}_{mdhv}, T^{mt}_{mdhv}, T^{pt}_{mdhv}\right)$$

$$\widetilde{T}^t_{mdhk} = \left(T^{ot}_{mdhk}, T^{mt}_{mdhk}, T^{pt}_{mdhk}\right)$$

$$\widetilde{T}_v = \left(T^o_v, T^m_v, T^p_v\right) \tag{34}$$

In the next stage, namely, an interactive fuzzy programming approach, to handle the multi-objective nature of the problems is introduced. Hence, an effective interactive fuzzy programming method is chosen to attain an effective solution. Various methods are been developed to handle the multi-objective nature of optimization problems such as the weighted sum approach, the constraint technique, the goal-programming approach, the fuzzy and the goal-programming techniques (Goodarzian & Hosseini-Nasab, 2019). Fuzzy programming and fuzzy decision making are two approaches that introduced by

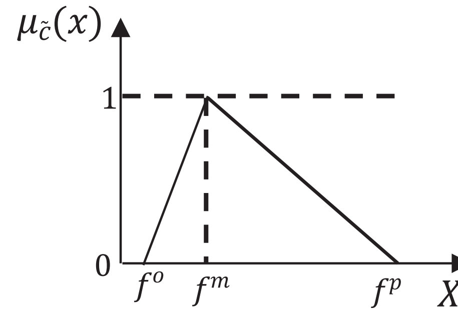

Fig. 2. A triangular fuzzy numbers.

Zimmermann (1978) and Bellman and Zadeh (1970), respectively, to solve multi-objective models. Both approaches tend to achieve the positive ideal solutions (PIS) and the negative ideal solutions (NIS) of the corresponding objective functions. These values are defined either by the DM's priorities (among the best and worst values of each function) or are equal to the best and worst values of each function as follows:

$$F^{PIS}_{1a} = Min\left(F^m_1\right) \tag{35}$$

$$F^{NIS}_{1a} = Max\left(F^m_1\right) \tag{36}$$

$$F^{PIS}_{1b} = Min\left(F^m_1 - F^o_1\right) \tag{37}$$

$$F^{NIS}_{1b} = Max\left(F^m_1 - F^o_1\right) \tag{38}$$

$$F^{PIS}_{1c} = Min\left(F^p_1 - F^m_1\right) \tag{39}$$

$$F^{NIS}_{1c} = Max\left(F^p_1 - F^m_1\right) \tag{40}$$

$$F^{PIS}_{2} = Min(F_1) \tag{41}$$

$$F^{NIS}_{2} = Max(F_1) \tag{42}$$

In this regard, each objective function is related to an equivalent linear MF in which achieved by utilizing equations (43)-(44).

$$\mu_{(x)} = \begin{cases} 1 if F \le F^{PIS} \\ \dfrac{F^{NIS} - F}{F^{NIS} - F^{PIS}} F^{PIS} \le F \le F^{NIS} \\ 0 if F \ge F^{NIS} \end{cases} \tag{43}$$

$$\mu_{(x)} = \begin{cases} 0 if F \le F^{NIS} \\ \dfrac{F^{NIS} - F}{F^{NIS} - F^{PIS}} F^{NIS} \le F \le F^{PIS} \\ 1 if F \ge F^{PIS} \end{cases} \tag{44}$$

The considerable advantages of interactive methods are relevant to their capability to present a systematic structure, enabling the DM to interactively adjust the parameters based on her/his priorities until an effective satisfactory solution achieved (El-Wahed & Lee, 2006). The utilized fuzzy programming approach in this study involves nine phases as below:

Phase 1: A proper pattern of the distribution of the triangular possibility for all uncertainty parameters and provide the fuzzy multi-objective MILP model is specified.

Phase 2: The fuzzy objective (the first objective function) into crisp ones, according to the explained process in the first stage is converted.

Phase 3: The optimization process is performed for each objective function. If the solutions attained from this stage are equal, hence chose one of them and transport to the DM and go to phase 9; Otherwise, continue and go ahead of the method on phase 4.

Phase 4: the attained solutions resulted from phase 3 and also the value of PIS related to each objective are considered, the NIS for each objective function to solve the MILP problem is determined.

Phase 5: the linear MF related to each objective function based on equations (43)–(44) is specified.

Phase 6: The multi-objective MILP problem into an equivalent MILP utilizing the following suggested auxiliary crisp formulation is transformed in equation (45) and solved.

$$\begin{aligned} & Max\eta(x) = \eta_0 + \phi\sum_{s=1}\varpi_s\eta_s \\ & S.t: \ \varpi_s(\eta_0) + \eta_s \leqslant \mu_s(x), \ s = 1\ldots S \\ & \qquad x \in F(x) \end{aligned} \tag{45}$$

where, $\mu_s(x)$ and ϕ shows the value of small positive and the satisfaction level of objective, which is typically set to be 0.01, respectively. Also, the sth objective relative importance is referred by ϖ_s that it is specified based on DM's priority as $\sum_s\varpi_s = 1, \varpi_s > 0$. Furthermore, the degree of compromise between the level of minimum satisfaction of objectives and the objectives is investigated by η_0 in the mentioned above formulation. x denotes the variables of decision, and $F(x)$ must be defined as feasible zone in which contains all the constraints.

Phase 7: The attained solution to the DM; if the solution associates with the priority of the DM is delivered, it would be considered as the solutions of compromise and go to phase 9. Otherwise, go to phase 8.

Phase 8: The model should be interactively modified based on DM's priority to attain the suitable solution. This procedure repeats until the method of solution leads to generate the solution of satisfactory. Likewise, the modifications based on the maximization of objectives, raise the NIS, while the reduction of objectives, minimize the PIS, and the modification of the sum weighted coefficients of the objective is permitted. Although any modification in the value of NIS leads a variation in the achieved outcome, also the size of the modified NIS should be as small as possible to avoid determining in the zone of infeasibility.

Phase 9: The condition of the stop, the procedure of fuzzy programming for the GMSCN model, has reached the solution of compromise.

5. Methodology solutions

Meta-heuristic algorithms indicate the main types of stochastic approaches (Dokeroglu et al., 2019). The types of algorithms can be utilized to speed up the process of obtaining a high-quality solution in cases where finding an optimal solution is very difficult. The main reasons for using the meta-heuristic algorithms divided into three including (i) for solving large problems, (ii) for making a more robust algorithm, and (iii) for solving of the problems faster. Also, these approaches are flexible and easy to implement as well as simple to design. Meta-heuristic optimization algorithms have become a well-known choice to solve complex problems which are otherwise difficult to solve by traditional approaches. Since meta-heuristic algorithms can solve multiple-solution, multiple-objective, and nonlinear formulations (Dokeroglu et al., 2019). In addition, to obtain high-quality solutions to an ever-growing number of complex problems are employed. In this regard, hybrid meta-heuristic algorithms have been developed by combining two or more algorithms to enhance or improve overall search performance and convergence. The advantages of the use of the proposed meta-heuristic algorithms in this paper are divided into five categories: (*i*) have a very fast rate of convergence and reduced computational time, (*ii*) are easy to implement, (*iii*) has the ability to handle random types of objectives and constraints, (*iv*) have the ability to converge to a true global optimum, and (*v*) they can be combined with other algorithms. The scopes of proposed meta-heuristic algorithms in this paper can be divided into many fields, including supply chain network (Goodarzian et al., 2020b), health care management (Goodarzian et al., 2021c), allocation-location problem (Bouchra et al., 2020), production-inventory-location-allocation problem (Janatyan et al., 2021), scheduling problem (Goodarzian et al., 2020b), supply chain finance, financial problems (Goli et al., 2020), etc.

Then, meta-heuristic algorithms can play a significant role in solving complex supply chains related to problems derived from the importance of designing and managing the entire supply chain. In the past, algorithms with stochastic components were often mentioned as a heuristic method, though the recent literature tends to refer to them as meta-heuristics (Ting et al., 2015). Therefore, we will follow Glover's convention and call all modern nature-inspired algorithms meta-heuristics (Glover & Sörensen, 2015). The word "meta-heuristic" was introduced by Fred Glover in his seminal paper. Also, he proved a meta-heuristic can be considered as a "master strategy that guides and modifies other heuristics to produce solutions beyond those that are normally generated in a quest for local optimality". In this regard, exact methods cannot achieve a good solution in a reasonable time in large-size problems, and also due to the complexity of the supply chain models, so meta-heuristic algorithms are used (Goodarzian et al., 2021a). Because of this, all meta-heuristic algorithms utilize a certain tradeoff of local search and randomization that cause quality solutions to difficult optimization problems can be found in a reasonable time (Ting et al., 2015; Dokeroglu et al., 2019).

Therefore, two new hybrid metaheuristic algorithms, namely, Hybrid Firefly algorithm (HFA) and Simulated Annealing (HFFA-SA) and Hybrid FFA and Social Engineering Optimization (HFFA-SEO) are developed here, which are introduced for the first time. In the next step, the results obtained from the HFFA-SA and HSEO-FFA algorithms are compared with other algorithms, including the original Social Engineering Optimization (SEO), the Improved Kill Herd (IKH), the Improved Social Spider Optimization (ISSO), and the Hybrid Whale Optimization and Simulated Annealing (HWOSA) algorithms. Likewise, the interested readers for more information on these algorithms can refer to (Guo et al., 2014) and (Nguyen & Vo, 2019), respectively. In the next section, HFFA-SA and HFFA-SEO algorithms explain thoroughly.

5.1. Multi-objective optimization

As it is discussed, the presented problem considered two various objective functions. The interactions among the solutions could be seen using the Pareto optimal set. This set involves non-dominated solutions (Goodarzian et al., 2020b). To describe this reality, two solutions are considered: solution F_1 and F_2. Solution F_1 dominate the Solution F_2 when all objectives of F_1 are not worse than F_2, and it is available when at least one of the solutions of F_1 is better than F_2 (Guo et al., 2014; Nguyen & Vo, 2019). According to the Pareto optimum set, this paper uses four assessment metrics to evaluate the quality of Pareto fronts, such as many new types of research, e.g. (Taghipour, 2018; Pech et al., 2019; Goodarzian et al., 2021d; Goodarzian et al., 2020b). In this regard, the solution representation of utilizing multi-objective meta-heuristic algorithms is explained in the following.

5.2. Solution representation

A scheme should be designed to encode the problem to implement the metaheuristic algorithms. According to this purpose, a two-stage method called Random-Key (RK) is utilized (Goodarzian et al., 2020a, 2020b). Therefore, this approach converts an unfeasible solution to a feasible one, by a set of methods in two stages (Devika et al., 2014). In recent years, researchers have used this method in many contents of engineering design. For more information about this topic, refer to references (Khodemani-Yazdi et al., 2019; Rahimi et al., 2019). Then, a numerical example to encode the solution representation is shown as follows. Consider that there are six internal and foreign manufacturing centers (*i, f*), six customers (*p, h*) with two types of vehicles (*v, k*), and fifteen pharmaceutical products (*m*). First of all, the sort of utilized vehicle system should be specified to send each product to customers. In this way, an array with a length of *C* is created by a uniform distribution: *U (0, c)*. Then, the sort of transportation system allocations to send each product to customers must be determined. Furthermore, a group of methods is shown in Fig. 3. Therefore, the third type of vehicle system is used for customers c_1, c_2, and c_3. Likewise, the fourth and sixth sort of vehicle systems are used for customers c_4 and c_6, respectively.

Therefore, an array with the length of *D* is distributed by *U (0,1)* to determine the route of the transportation vehicle system of products to customers. In the second stage, these numbers are sorted. In the next step, these numbers are specified to schedule the delivery of products to the customers. Fig. 4 indicates an instance of the utilized arrays of this matrix for algorithms. Primarily, based on the maximum optimal total traveled distance, the capacity of the utilized vehicle system, as well as delivered products to the customers' constraints, the route of five utilized vehicle systems for shipping products to the customers, are checked and determined. According to this instance, the sixth customer is not needed for the routes. These routes are shown as follows:

$$c_1 = \{d_2 \to d_8 \to d_{11}\},\ c_2 = \{d_{14} \to d_1 \to d_{13}\},\ c_3 = \{d_7 \to d_5 \to d_{10}\},$$
$$c_4 = \{d_{12} \to d_4\},\ c_5 = \{d_6 \to d_9\}$$

5.3. Hybrid firefly algorithm and simulated Annealing (HFFA-SA)

The exploitation and exploration process must be well-balanced in a robust search process. The exploration is the capability of research into the different obscure areas in the problem to find a Pareto optimal response, ideally, the globally optimum one. However, the exploitation is the capacity of focusing on the search around a promising candidate solution to discover the optimal answer. Exploration and exploitation are two terms on the opposite side of each other. To reach optimal performance, these two features should be well balanced. In addition, Goodarzian and Hosseini-Nasab (2019) mentioned that more exploitation may lead to early convergence while too much exploration may hinder the convergence time. Considering FFA declares that the exploration is not rigorous enough during the early stage. However, during late cycles, the exploration is not required if the FFA uncovers the appropriate part of the search area. As investigated in Goodarzian et al. (2020b), the SA has a superior convergence ability because of big jumps of the *le*Ávy flight procedures. So, the FFA and SA are synthesized to ameliorate global search capability. Moreover, to adjust the exploration process, the "exploration breakpoint" (EBP) control parameter is suggested here.

The FFA is a population-based algorithm, inspired by the communication behavior of fireflies and the flashing, and first presented by Yang (2010). FFA includes three glorified features: (*i*) The less bright firefly moves towards a brighter firefly. The attractiveness of one firefly towards another, specified by the brightness, is inversely proportional to the distance; (*ii*) The brightness of a firefly is influenced or specified by the landscape of the objective function; (*iii*) All fireflies are unisex so that one firefly will be absorbed to other fireflies regardless of their sex.

The SA algorithm is introduced by Kirkpatrick et al. (1983), which is a stochastic, neighborhood-based search, iterative approach motivated from an analogy among the strategy of solving combinatorial optimization problems and the simulation of the annealing of solids. In the SA, a random search in terms of a Markov chain is used. Subsequently, the function of the neighborhood was described as a random walk with *le*Ávy flight such that the search process has better efficiency in Pavlyukevich (2007). Eventually, according to the above mentions, the HFFA-SA pseudo-code is indicated in Fig. 5.

5.4. Hybrid firefly algorithm and social engineering optimization (HSEO-FFA)

FFA algorithm is roused by fireflies, a sort of insect in nature. Most fireflies create short flashes and rhythmic. Sort of flashes is frequently exceptional for a particular kind. Glimmering light is created by a bioluminescence procedure, and its genuine capacity is as yet a matter of discussion between analysts. Fireflies utilize their substance light appeal for correspondence, chasing, and cautioning their adversaries (Yang, 2010). Light intensity (*I*) at a specific distance (*r*) from a light source is specified by inverse square law. In this manner, a light diminishes as the separation increases. Furthermore, the air ingests light, and its force diminishes and gets more vulnerable as separation increments. Consequently, most fireflies are able to see from a constrained separation of two or three hundred meters, and it is typically a palatable separation for fireflies to impart. In this manner, blazing light can be planned as the target capacity to be improved, so it gives another population-based FFA (Yang, 2010). Based on the inverse square law, a light intensity ($I(r)$) at r distance from a light source (l_s) is computed in Eq. (46).

$$I(r) = l_s / r^2 \tag{46}$$

Hence, light is attracted in an environment by a constant light absorption coefficient (γ) $\in [0, \infty)$. Afterward, the equation is formulated in Gaussian in Eq. (47)

$$B(r) = B_0 e^{-\gamma r^2} \tag{47}$$

where B_0 is attractiveness when $\boldsymbol{r} = 0$ and $B(r)$ is the attractiveness of a firefly at $\boldsymbol{r}$ distance.

In the SEO algorithm, with two random solutions, which are the best solution, namely the attacker defender is started. In this manner, to

c_1	c_2	c_3	c_4	c_5	c_6	
1.26	1.67	1.39	0.56	2.14	0.87	**Step1:** Initialize the random numbers
2	2	2	1	3	1	**Step2:** Round the numbers to the near greatest value.

Fig. 3. The utilized procedure to allocate a sort of vehicle system for customers.

d_1	d_2	d_3	d_4	d_5	d_6	d_7	d_8	d_9	d_{10}	d_{11}	d_{12}	d_{13}	d_{14}	
0.25	0.03	0.59	0.78	0.35	0.89	0.31	0.09	0.97	0.46	0.12	0.61	0.29	0.17	**Step 1:** Initialize the random numbers
5	1	10	12	8	13	7	2	14	9	3	11	6	4	**Step 2:** Sort and determine numbers

Fig. 4. The utilized method to allocate transportation systems to deliver products to customers on each route.

```
%% HFFA-SA Algorithm Parameters
%%HFFA-SA parameters
MaxIt=500;        % Maximum Number of Iterations
MaxSubIt=10;      % Maximum Number of Sub-iterations
T0=10;            % Initial Temp.
alpha=0.99;       % Temp. Reduction Rate
nPop=40;          % Number of Fireflies (Swarm Size)
gamma=1;          % Light Absorption Coefficient
beta0=2;          % Attraction Coefficient Base Value
alpha=0.2;        % Mutation Coefficient
```

```
alpha_damp=0.99;   % Mutation Coefficient Damping Ratio
delta=0.05*(VarMax-VarMin);    % Uniform Mutation Range
m=2;

%% Initialization
 % Empty Firefly Structure
firefly.Position=[];
firefly.Cost=[];

% Initialize Population Array
pop=repmat(firefly,nPop,1);

% Initialize Best Solution Ever Found
BestSol.Cost=inf;

% Create Initial Fireflies
for i=1:nPop
  pop(i).Position=unifrnd(VarMin,VarMax,VarSize);
  pop(i).Cost=CostFunction(pop(i).Position);

  if pop(i).Cost<=BestSol.Cost
     BestSol=pop(i);
  end
end

% Array to Hold Best Cost Values
BestCost=zeros(MaxIt,1);
 % Initialize Temp.
T=T0;

%% HFFA-SA Algorithm Main Loop

for it=1:MaxIt
  for subit=1:MaxSubIt

   newpop=pop;
   for i=1:nPop
      for j=1:nPop
         if pop(j).Cost<=pop(i).Cost
            rij=norm(pop(i).Position-pop(j).Position);
            beta=beta0*exp(-gamma*rij^m);
            e=delta*unifrnd(-1,+1,VarSize);
            %e=delta*randn(VarSize);

            newpop(i).Position=pop(i).Position...
               +beta*(pop(j).Position-pop(i).Position)...
               +alpha*e;
            newpop(i).Position=max(newpop(i).Position,VarMin);
            newpop(i).Position=min(newpop(i).Position,VarMax);
            newpop(i).Cost=CostFunction(newpop(i).Position);

            if newpop(i).Cost<=BestSol.Cost
               BestSol=newpop(i);
            end
         end
      end
   end

   % Merge
   pop=[pop
      newpop
      BestSol];  %#ok

   % Sort
   [~, SortOrder]=sort([pop.Cost]);
   pop=pop(SortOrder);
```

Fig. 5. The pseudo-code of proposed HFFA-SA.

evaluate the learner's retraining and training from the attacker to the defender, a set of experiments is described for each trait that the attacker experiments a trait in the defender and the amount of learning is computed and the fresh defender has the highest rate of re-training if there is a substitution for the current defender. Moreover, attacks from the are completed by the methods that are accessible to him/her. In the process, the defender moves to the attacker's points to react to the attacks and the defender is estimated and this procedure is replicated until

```
% Truncate
pop=pop(1:nPop);
 % Compare using SA Rule
   for i=1:nPop

      if newpop(i).Cost<=pop(i).Cost
         pop(i)=newpop(i);
      else
         DELTA=(newpop(i).Cost-pop(i).Cost)/pop(i).Cost;
         P=exp(-DELTA/T);
         if rand<=P
            pop(i)=newpop(i);
         end
      end

% Store Best Cost Ever Found
BestCost(it)=BestSol.Cost;

% Show Iteration Information
disp(['Iteration ' num2str(it) ': Best Cost = ' num2str(BestCost(it))]);

% Damp Mutation Coefficient
alpha=alpha*alpha_damp;
% Temp. Reduction
T=alpha*T;
    end
 end
end
```

Fig. 5. (*continued*).

the end of the attack. If the defenders' value would be higher than the attacker, they are substituted by each other. In the end, a fresh defender reboots the algorithm. In the SEO, similar to other metaheuristics, the stages of the search are provided. Additionally, the retraining and training of the defender and the attacker form a local search in the SEO. Moreover, the attackers' strikes on the defender and the reaction to that concentrate stage are organized. Finally, the selection of the fresh defender will be the stage of diversity of the SEO (Fathollahi-Fard et al., 2018). Fig. 6 shows the pseudo-code HSEO-FFA algorithm. The implementation steps of the SEO algorithm are explained as follows.

- Initialize the defender and the attacker
- Training and retraining
- Spot an attack
- At this stage, in order to carry out an attack, this research proposes four various techniques, including obtaining, phishing, diversion theft, and pretext.
- Respond to attack
- Choose a novel person as a defender
- Stop condition

6. The numerical computation and results

In this section, the efficiency and performance of the proposed model are investigated. According to the novelty of the proposed GMSCN model, no existing study has treated a similar model in the literature. Moreover, the available benchmarks in the literature are not existing in the proposed model and not available real data for the presented model. Then, an approach is required to design the test problems. Numerical instances in the various sizes, including small-sized and large-sized problems, are considered. The problem size is determined according to the characteristics such as IPC, FPC, DC, the customer (pharmacy and hospital), vehicle type (airplane and Nissan, and pickup truck), routes, pharmaceutical product, and finally the period. Also, different sizes of the problem are indicated in Table 2.

The convergence quality of the evolutionary algorithm solution highly depends on the setting of the algorithm's parameters (Goodarzian & Hosseini-Nasab, 2019). Therefore, proper algorithm parameters are necessary to avoid bad simulation results. The scientific methods of setting the parameters of metaheuristic algorithms in the literature are infrequent and dependent on the experience of the researchers (Lee, 2018). Also, the comprehensive analysis of all possible combinations of the parameter is inaccessible. Hence, the values of the appropriate parameters that obtained good performance are determined after running multiple analyzes and analyzing different aspects of the problem using the proposed algorithms. The efficiency of the suggested meta-heuristics in each of the 10 problem examples is investigated on various parameters according to the various values of each parameter. Therefore, the parameters of the presented model are listed in Table 3 as well as the values of the parameter setting of the algorithms are indicated in Table 4.

According to Tables 2 and 3, the size of the problem is changed, but the nature of the problem is not changed. Therefore, the GMSCN model is always feasible based on these changes. To better explain, a few constraints are investigated to clarify the feasibility of the proposed model and the satisfaction of constraints. In this example, based on the constraints (10)-(18), SP1 test, and Table 3 are investigated as follow:

$$\sum_{t=1,m=3,d=2} IL^{t}_{md} = 3000 \tag{48}$$

$$\sum_{m=3}\sum_{i=1}\sum_{d=2}\sum_{t=1}\sum_{r=1} N^{tr}_{midv} \leqslant 250000 \tag{49}$$

$$\sum_{m=3}\sum_{i=1}\sum_{d=2}\sum_{t=1}\sum_{r=1} N^{tr}_{midk} \leqslant 250000 \tag{50}$$

$$\sum_{m=3}\sum_{f=1}\sum_{i=1}\sum_{t=1}\sum_{r=1} N^{tr}_{mfiv} \leqslant 200000 \tag{51}$$

$$\sum_{m=3}\sum_{d=2}\sum_{p=2}\sum_{t=1}\sum_{r=1} N^{tr}_{mdpv} \leqslant 150000 \tag{52}$$

$$\sum_{m=3}\sum_{d=2}\sum_{p=2}\sum_{t=1}\sum_{r=1} N^{tr}_{mdpk} \leqslant 250000 \tag{53}$$

```
%% HSEO-FFA Algorithm Parameters
%%HSEO-FFA parameters
MaxIt=25;     %Maximum number of iteration

alpha=0.2;      %Rate of collecting data
betta=0.08;      %Rate of connecting attacker
Num_C=50;       %Number of connections
nPop=40;          % Number of Fireflies (Swarm Size)
gamma=1;          % Light Absorption Coefficient
beta0=2;         % Attraction Coefficient Base Value
alpha=0.2;        % Mutation Coefficient
alpha_damp=0.99;    % Mutation Coefficient Damping Ratio
delta=0.05*(VarMax-VarMin);     % Uniform Mutation Range
m=2;

%% Initialization
time1=clock;
person_individual.Position=[];  % the traits of each person
 person_individual.Cost=[];      % attribute of ability in each person
 person=repmat(person_individual,1,2);

for i=1:2
    person(i).Position=unifrnd(VarMin, VarMax, VarSize);
    person(i).Cost=CostFunction(person(i).Position);
end

costs=[person.Cost];
 [~, index]=sort(costs);
 person=person(index);
 attacker=person(1);   %selecting attacker
 defender=person(2);   %selecting defender
 gamma=round(nVar*alpha);
tetta=zeros(1,gamma);
sigma = 0.1*(VarMax-VarMin);

% Create Initial Fireflies
for i=1:nPop
   pop(i).Position=unifrnd(VarMin,VarMax,VarSize);
   pop(i).Cost=CostFunction(pop(i).Position);

   if pop(i).Cost<=BestSol.Cost
      BestSol=pop(i);
   end
end
BestCost=zeros(MaxIt, 1);
it=1;

%% HSEO-FFA Main Loop

   %% Training and retraining
   person_evaluator=repmat(defender,1,gamma);

   for i=1:gamma
      random_number=randi([1, nVar]);
       person_evaluator(i).Position(random_number)=attacker.Position(random_number);
      person_evaluator(i).Cost=CostFunction(person_evaluator(i).Position);
      tetta(i)=defender.Cost-person_evaluator(i).Cost;
   end

   [value, index]=max(tetta);

   if person_evaluator(index).Cost<defender.Cost
      defender=person_evaluator(index);
   end

   %% Spotting a social engineering attack
   for j=1:Num_C
   new_defender.Position=Connect(defender.Position,defender.Position,betta,VarMin,VarMax);
   new_defender.Position=Connect(new_defender.Position,attacker.Position,betta,VarMin,VarMax);
   new_defender.Cost=CostFunction(new_defender.Position);
```

Fig. 6. The pseudo-code of proposed HSEO-FFA.

$$\sum_{m=3}\sum_{d=2}\sum_{h=2}\sum_{t=1}\sum_{r=1}N^{tr}_{mdhv}\leqslant 200000 \tag{54}$$

$$\sum_{m=3}\sum_{d=2}\sum_{h=2}\sum_{t=1}\sum_{r=1}N^{tr}_{mdhk}\leqslant 150000 \tag{55}$$

$$\sum_{m=3}\sum_{p=2}\sum_{h=2}\sum_{t=1}\sum_{r=1}N^{tr}_{mphk}\leqslant 250000 \tag{56}$$

Based on the above example, we do for all constraints. Then, all variable decisions are obtained. According to obtained variable decisions and parameters, the obtained values are placed in the objective function until the values of the objective function are obtained.

The IKH algorithm is a random and inspired nature that is used as a solving method in optimization problems. The IKH algorithm is classified as a swarm intelligence algorithm. The efficiency of the IKH algorithm is analyzed by weak exploitation capability. In this study, we

```
%% Responding to Social engineering attack
  if new_defender.Cost<defender.Cost
  defender=new_defender;
end

if defender.Cost< attacker.Cost
        attacker=defender;
end
end
%% Hitting to defender
  defender.Position=unifrnd(VarMin, VarMax, VarSize);
  defender.Cost=CostFunction(defender.Position);

%% Stop Condition
BestCost(it)=attacker.Cost;
```

Fig. 6. (*continued*).

Table 2
The different sizes of the test problems.

Problem size		i, f	d	p, h	v	k	m	t	r
Small	**SP1**	1	2	2	1	1	3	1	1
	SP2	2	2	4	1	1	4	1	1
	SP3	3	3	4	2	2	5	2	1
	SP4	3	4	5	2	3	4	2	1
	SP5	4	4	6	3	3	6	3	1
	SP6	4	4	5	4	2	6	2	2
	SP7	6	5	5	5	3	5	3	2
	SP8	6	4	4	6	2	6	2	2
	SP9	6	5	5	7	3	6	3	2
	SP10	7	5	6	7	4	6	3	2
Large	**LP1**	8	6	7	10	3	7	4	2
	LP2	10	7	8	14	4	8	6	2
	LP3	20	8	9	18	4	9	6	2
	LP4	30	10	10	22	5	9	8	2
	LP5	40	12	16	26	5	10	8	3
	LP6	40	14	20	30	3	10	10	3
	LP7	50	16	40	34	4	11	10	3
	LP8	60	18	60	38	4	11	10	4
	LP9	80	20	80	42	5	12	11	4
	LP10	100	22	80	46	6	14	12	4

proposed an IKH algorithm by building a global search capability. In addition, this algorithm has a high convergence rate. Also, the ISSO algorithm is used, which is very powerful in finding Pareto optimal publicity and convergence. The ISSO algorithm is able to select the minimum number of sensors in the sensor set by finding the Pareto optimal solutions and fast approaching convergence. The ISSO algorithm has a strong convergence due to sudden changes in the movement of search factors during the early stages of optimization. This factor helps the metaheuristic algorithms in exploring the search space. Furthermore, the HWOSA due to its simplicity and high efficiency to solve hybrid optimization problems, this algorithm obtained a special place among search techniques and heuristic methods. This algorithm is a random method that uses the statistical mechanism to obtain a Pareto optimal solution. However, the SEO algorithm is an intelligent approach that is inspired by social engineering rules and simulated as an emerging phenomenon in the real world today. The SA algorithm is a simple and efficient meta-heuristic optimization algorithm to solve optimization problems in a big search space. This algorithm is mostly used when the search space is discrete, and often utilized to estimate "Pareto optimal solutions" in optimization problems whose search space is large. Nature-inspired algorithms are among the most potent "optimization" methods. Here, an optimization algorithm, namely the FFA is examined. An essential feature of the FFA, which distinguishes it from some similar optimization meta-heuristics, is its excellent efficiency in searching for Pareto optimal solutions relevant to multiple modality problems and functions. Such a significant feature in the FFA algorithm has made it an ideal choice for multimedia optimization applications.

The proposed model is simulated on the GAMS 24. 1. 3 and MATLAB R2020 b software on a computer with Intel (R) Core (TM) i5.2400 2.50 GHz in CPU and 6 GB memory on the Windows 8.1 platform. The obtained results from the utilized metaheuristic algorithms and the computational (CPU) time of each solution are noted in Tables 5 and 6 for 10 samples of small- and large-scale problems respectively.

To survey the impact of the total costs and environmental on the GMSCN, the IKH, ISSO, HWOSA, SEO, HSEO-FFA, and HFFA-SA algorithms are used. The results are portrayed in Fig. 7. As illustrated in Fig. 7, the total costs and the environmental impacts are increasing along with rising the problem size. In Fig. 7a, it can be seen that as the size of the problem increasing, the objective functions (F1 and F2) are increasing too. Therefore, the results obtained of objective functions (F1 and F2) of MILP in the GAMS software are better than other algorithms in small-sized problems. In addition, the HSEO-FFA algorithm shows better efficiency and performance than other metaheuristic algorithms in large-sized problems. After the results of MILP, the developed algorithm in this paper, has a better solution than the other IKH, ISSO, HWOSA, and HFFA-SA algorithms.

In this way, as it is obtained from Fig. 7b. when the size of the

Table 3
The values of used parameters in the numerical experiments.

Parameters	Value/distribution	Parameters	Value/distribution
$\widetilde{C}^t_{im}$,$\widetilde{C}^t_{fm}$,$\widetilde{C}^t_{dm}$	$\tilde{U}(25,35)$, $U(35,45)$,$U(45,55)$	π_v	$\tilde{U}niform(500,2000)(KM)$
β_p,β_h	100000	EP^t_{md}	$\tilde{U}niform(100000,200000)$
d_{id},d_{fi},d_{dp},d_{dh},d_{ph}	$\tilde{U}niform(5,3000)km$	μ	$\tilde{U}niform(150,200)$
P^t_m,P^t_{mi},P^t_{mf},L^t_m	$\tilde{U}niform(500,1500)$	δ_{dpm},δ_{dhm}	150
$\widetilde{T}^t_{midv}$,$\widetilde{T}^t_{midk}$,$\widetilde{T}^t_{mfiv}$,$\widetilde{T}^t_{mdpv}$,$\widetilde{T}^t_{mdpk}$,$\widetilde{T}^t_{mdhv}$,$\widetilde{T}^t_{mdhk}$,$\widetilde{T}^t_{mphk}$	$\tilde{U}(15,20)\$$, $U(20,25)$, $U(25,30)$	K^t_{mdi},K^t_{mif},K^t_{mpd},K^t_{mhd},K^t_{mph}	$\tilde{U}niform(15000,25000)$
IL^t_{dm}	$\tilde{U}niform(300000,500000)$	θ_p,θ_h	$\tilde{U}niform(15,25)$
ϕ_d,ϕ_v,ϕ_k,ϕ_p,ϕ_h	$\tilde{U}niform(150000,250000)$	J^t_{md},I^t_{md}	$\tilde{U}niform(20000,30000)$
MAX	3000000	σ_{vk}	$\tilde{U}niform(20000,30000)$
S^t_{mdi},S^t_{mif},S^t_{mpd},S^t_{mhd},S^t_{mph}	$\tilde{U}niform(300000,500000)$	Big M	100000000

Table 4
Values of parameter setting of the algorithms.

Algorithms	Parameters	Parameter setting									
		1	2	3	4	5	6	7	8	9	10
SEO	Max Iteration	50	75	100	125	150	175	200	225	250	300
	Num_C(Number of connections)	50	75	100	125	150	175	200	225	250	300
	α(collecting data rate)	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55	0.6	0.65
	β(connecting attacker rate)	0.5	0.55	0.65	0.7	0.75	0.8	0.85	0.9	0.95	0.99
HWOSA	Max Iteration	50	75	100	125	150	175	200	225	250	300
	T_0	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55
	P(acceptability probability function)	0.25	0.3	0.35	0.4	0.45	0.5	0.55	0.6	0.65	0.7
	Number of search agents	30	40	50	60	70	80	90	100	110	120
IKH	Max Iteration	50	75	100	125	150	175	200	225	250	300
	Maximum induced speed	10	15	20	25	30	35	40	45	50	55
	Inertia weight of the motion induced	0.3	0.4	0.45	0.5	0.6	0.65	0.7	0.75	0.8	0.9
	Foraging speed	25	35	45	55	65	75	85	95	105	115
	Maximum diffusion speed	12	14	16	18	20	22	24	26	28	30
	Crossover rate	0.2	0.3	0.35	0.4	0.5	0.55	0.6	0.7	0.75	0.8
	Mutation rate	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55
ISSO	Max Iteration	50	75	100	125	150	175	200	225	250	300
	Npop	100	150	200	250	300	350	400	450	500	550
	vibration intensity	25	50	75	100	125	150	175	200	225	250
	W_s(the weight of a typical spider)	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55
	Domain of research	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55
	coefficient attract	0.3	0.35	0.4	0.45	0.5	0.55	0.6	0.65	0.7	0.75
HSEO-FFA	Max Iteration	50	75	100	125	150	175	200	225	250	300
	Collecting data rate	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55	0.6	0.65
	connecting attacker rate	0.02	0.03	0.04	0.045	0.05	0.06	0.065	0.07	0.075	0.08
	Number of connections	50	60	70	80	90	100	120	140	160	180
	Fireflies Number (The size of swarm)	40	60	80	100	120	140	160	180	200	220
	The Coefficient of Light Absorption	1	2	2.5	3	3.5	4	4.5	5	5.5	6
	The Value of Attraction Coefficient Base	2	2.5	3	3.5	4	4.5	5	5.5	6	8
	The Coefficient of Mutation	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55	0.6	0.65
	The ratio of mutation coefficient damping	0.15	0.25	0.35	0.4	0.5	0.6	0.65	0.75	0.85	0.99
	The range of uniform mutation	0.1	0.2	0.3	0.4	0.5	0.55	0.6	0.7	0.8	0.9
HFFA-SA	Max Iteration	50	75	100	125	150	175	200	225	250	300
	Initial Temp.	10	15	20	25	30	35	40	45	50	60
	Temp. Reduction Rate	0.15	0.2	0.3	0.4	0.5	0.6	0.7	0.85	0.9	0.99
	Maximum Number of Sub-iterations	50	60	70	80	90	100	120	140	160	180
	Number of Fireflies (Swarm Size)	40	60	80	100	120	140	160	180	200	220
	Light Absorption Coefficient	1	2	2.5	3	3.5	4	4.5	5	5.5	6
	Attraction Coefficient Base Value	2	2.5	3	3.5	4	4.5	5	5.5	6	8
	Mutation Coefficient	0.2	0.25	0.3	0.35	0.4	0.45	0.5	0.55	0.6	0.65
	The ratio of mutation coefficient damping	0.15	0.25	0.35	0.4	0.5	0.6	0.65	0.75	0.85	0.99
	The range of uniform mutation	0.1	0.2	0.3	0.4	0.5	0.55	0.6	0.7	0.8	0.9

problem is increased, the objective functions (F1 and F2) computed by IKH, ISSO, HWOSA, SEO, HSEO-FFA, and HFFA-SA algorithms on the large-sized problem are risen gradually, respectively. Therefore, the obtained results of objective functions (F1 and F2) of the HSEO-FFA algorithm are better and more robust than IKH, ISSO, HWOSA, SEO, and HFFA-SA algorithms on the large-sized problem. Also, the MILP shows better efficiency and performance than other methods in small-sized problems. After the results of MILP, both proposed algorithms have a better solution in comparison with the other IKH, ISSO, HWOSA, original SEO algorithms. As a result, the worst solution than other methods is the HWOSA algorithm in the different sizes of the problem. By rising the size of the problem, the results of the objective functions than the other methods are increased.

6.1. Evaluation metrics for Pareto optimum solutions

The comparison of multi-objective meta-heuristics is always problematic. Therefore, scholars have proposed a number of approaches to assess the quality of Pareto fronts for meta-heuristics (Goodarzian & Hosseini-Nasab, 2019; Goodarzian et al., 2021b; 2021e; 2021d). In this paper, four famous evaluation metrics are considered, including (*i*) the Maximum Spread (MS), (*ii*) Spread of Non-Dominance Solution (SNS), (*iii*) Mean Ideal Distance (MID), and (*iv*) Number of Pareto Solution (NPS) are used in this paper. In recent papers, these metrics were utilized in Goodarzian et al. (2021b).

6.2. Pareto optimal analysis: Comparison of algorithms

According to the proposed four evaluation metrics of Pareto optimum analyses, metaheuristic algorithms are compared together. To improve the efficiency of used meta-heuristic methods, the prior solutions are generated. According to the four algorithms involving IKH, ISSO, HWOSA, SEO, HSEO-FFA and HFFA-SA algorithms, their primary solutions are generated with an equal share. Eventually, to improve the reliability of metaheuristic algorithms, the average results for twenty-five run times are considered to utilize during this section. The behavior of meta-heuristic methods for the term of solution time is indicated in Fig. 8. From Fig. 8 and Table 5, it is evident that the HSEO-FFA is swifter than other metaheuristics. Thus, the CPU time of HSEO-FFA is less than other proposed metaheuristics on different scales. Therefore, HSEO-FFA has a minimum average of computational time (1913.408 s). The HWOSA has the maximum rate of this item (3256.667 s). Furthermore, Fig. 8 presents the computational time outcomes of the algorithms and the obtained outcomes by GAMS Software. The

Table 5
The obtained results from each proposed method in the different size of test problems.

Problem size	Objective function	MILP	SEO	HWOSA	IKH	ISSO	HFFA-SA	HSEO-FFA
SP1	F_1	2775661.32	5234341.222	6732437.34	5443112.322	5012213.566	4978054.05	4611223.05
	F_2	3221145.76	6733841.223	8995657.34	6344217.86	5677712.344	5467712.12	5122030.12
SP2	F_1	2887665.16	5844339.902	7955341.822	5607661.45	5233124.56	5143715.12	4886711.34
	F_2	3566711.43	7945599.902	9633231.822	6775664.23	5966703.43	5668912.56	5466533.23
SP3	F_1	2996765.45	6422670.811	8867143.819	5899122.21	5432211.17	5389946.32	4977541.18
	F_2	3801223.35	6883540.811	14649683.819	7105671.56	6322134.76	5850344.25	5654432.17
SP4	F_1	3122541.18	7935636.814	9457674.16	6176651.21	5634421.56	5567321.52	5122341.4
	F_2	4112567.18	14378386.944	24552544.58	13342521.56	11774321.5	10843123.27	9865543.14
SP5	F_1	3522176.13	11832231.78	14562261.94	10521131.23	9707655.34	8632298.23	7476651.23
	F_2	4776651.78	18446621.78	27847821.94	17766512.12	13512331.16	12332161.7	11122766.3
SP6	F_1	3887665.19	14623544.76	19734745.09	12836451.17	12156611.76	8960887.21	7867743.38
	F_2	5122345.18	24554124.76	32658462.05	20121801.18	17665443.2	14204216.75	12566322.67
SP7	F_1	4012276.56	16767887.21	23353401.77	15036567.6	14554302.7	9213544.21	8113677.78
	F_2	5663221.05	36443467.21	41478012.45	24516603.67	18866521.1	17543543.78	15966543.21
SP8	F_1	4334788.18	23981255.71	31666871.67	18324561.63	16890655.29	9376631.32	8456601.56
	F_2	5988711.65	43523755.71	57797819.34	29747651.17	21155601.67	19135642.73	17134451.45
SP9	F_1	4578823.05	28133133.514	36771212.677	21515801.23	17012455.12	9589932.71	9108771.2
	F_2	6123345.17	48134443.514	62276782.451	33634401.65	243455601.2	21463421.65	19466701.07
SP10	F_1	4788023.66	33515442.681	40573253.566	25233154.67	19233701.14	9756774.19	9412234.17
	F_2	6367719.18	50855852.681	63994433.566	37554591.23	27665433.12	24834421.3	23856701.03
LP1	F_1	–	29804561.01	42345510.34	27608711.2	21564431.3	9930998.21	9678891.3
	F_2	–	53566711.9	67023441.32	40355671.1	30245677.1	28,321,987	25,677,801
LP2	F_1	–	31220431.34	45660877.23	29,677,065	24567781.2	13536771.21	10234331.3
	F_2	–	56702331.45	70334211.4	43677811.07	34,566,780	31965543.54	28987721.4
LP3	F_1	–	34566088.3	48909812.45	32276551.12	26788011.1	14548713.4	13445011.3
	F_2	–	58234401.32	73455612.4	47890012.3	37890991.4	33,858,913	31,255,611
LP4	F_1	–	37588901.2	50344560.2	35678990.1	28,567,732	17590096.84	16557013.1
	F_2	–	60345011.4	75660734.3	49877601.4	41235667.71	37654421.74	35678890.1
LP5	F_1	–	41233401.5	52378906.2	37,899,054	31267889.6	19062561.31	17663210.2
	F_2	–	64566710.3	78066785.4	53455678.1	45,677,321	39181234.34	37880231.2
LP6	F_1	–	45667034.3	54,789,023	39567601.5	33456011.17	22324809.21	19024531.42
	F_2	–	67880238.21	80345561.6	56670231.3	48,908,761	46,843,321	41,566,744
LP7	F_1	–	47322011.34	57084431.4	41,233,406	36707661.2	24543527.9	22312567.01
	F_2	–	70122349.01	83455601.6	58098871.45	51,233,491	48764321.8	44566781.14
LP8	F_1	–	50125567.76	5,923,341	43556710.2	38788341.3	31706523.4	26789971.36
	F_2	–	73445610.19	86078891.3	61,233,207	53,455,676	51126788.45	50124451.31
LP9	F_1	–	53455061.4	61234556.4	45677801.9	40234566.5	34054327.6	29056771.2
	F_2	–	75,098,811	88045567.4	64566712.1	55607651.12	54,092,381	53,677,086
LP10	F_1	–	57034421.5	64506511.5	48900543.1	42,345,671	38967321.36	32445110.27
	F_2	–	78945651.18	90234456.8	68345521.6	58908871.7	56718932.4	55567102.28

Table 6
The CPU time results of the proposed methods in the different size of test problems.

Problem size	MILP	SEO	HWOSA	IKH	ISSO	HFFA-SA	HSEO-FFA
SP1	13.2	17.56	23.5	21.45	19.4	16.12	15.67
SP2	18.3	23	31.65	28.56	25.23	20.02	17.34
SP3	22.3	29.45	45.58	35.01	30.01	27.32	26.1
SP4	45	58.03	76.77	45.51	39.4	37.29	31.45
SP5	68.8	77.04	91.5	57.87	46.78	42.78	39.67
SP6	87.56	144.76	177.4	134.67	122.45	103.45	96.231
SP7	158.34	198.35	278.5	183.45	169.56	168.21	161.23
SP8	188.34	289.34	456.3	251.67	223.04	213.78	202.56
SP9	223.67	356.23	677.34	276.23	245.27	234.78	215
SP10	286.7	462.56	899.27	345.34	298.56	278.56	245.8
LP1	–	782.45	1023.67	703.58	688.2	635.26	601.45
LP2	–	1123.34	1344.56	1056.34	976.451	867.23	732.71
LP3	–	1556.32	1890.76	1306.23	1267.04	1189.34	1103.28
LP4	–	1866.38	2444.56	1678.26	1435.65	1324.67	1209.23
LP5	–	2123.56	2777.56	1967.26	1784.34	1541.31	1356.08
LP6	–	2677.6	3234.56	2478.71	2123.45	2098	2045
LP7	–	3256.56	3978.45	2956.21	2678	2480.32	2245.58
LP8	–	3788.9	4832.67	3361.06	2988.04	2891.45	2766.23
LP9	–	4233.2	5305.32	3967.25	3577.43	3489.21	3240.32
LP10	–	4889.23	5734.56	4561.67	4023.56	3971.67	3834.2

computational time of the MILP model in the small-sized problem is less than IKH, ISSO, HWOSA, SEO, HSEO-FFA, and HFFA-SA algorithms. Besides, the CPU time of the HWOSA algorithms increases with growing the size of the problems. After that, the HSEO-FFA algorithm than the other algorithms show less CPU time and more efficient in the small-sized problems. However, due to the complexity of the model and the NP-hard of the problem, the solution of the model in the GAMS software is not responding with raising the problem size. For this reason, we have used metaheuristic algorithms in the large-sized. Also, the HSEO-FFA algorithm in the large-sized increases with increasing CPU time of the

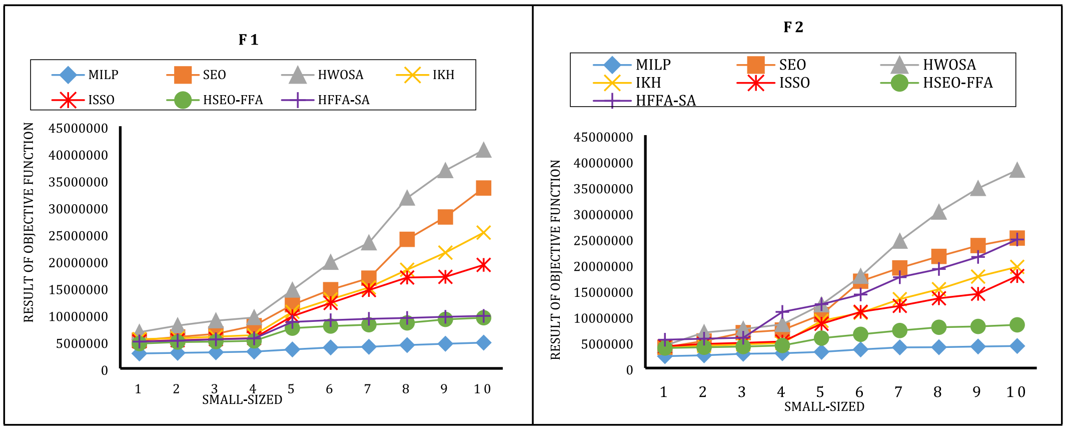

Fig. 7a. The behavior of the objective functions in the small-sized problems.

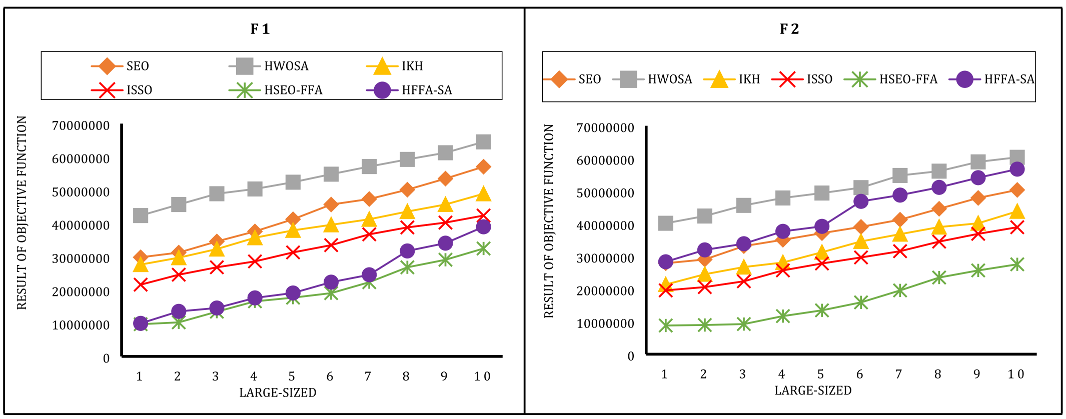

Fig. 7b. The behavior of the objective functions in the large-sized problems.

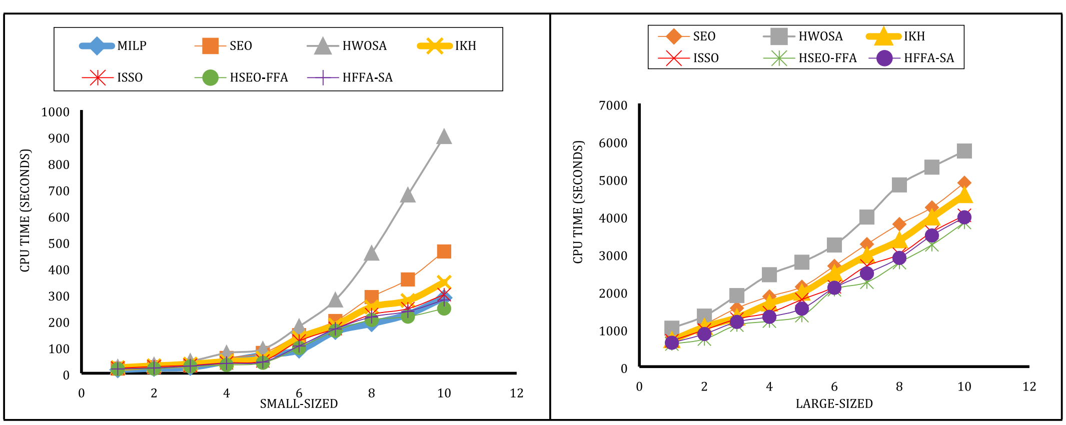

Fig. 8. The result of the CPU time in the different size problem.

problem. Furthermore, the HSEO-FFA algorithm requires less time to implement the model rather than the other algorithms in the large-sized problems.

The efficiency of the algorithms is examined by evaluation metrics, including MID, SNS, NPS, and MS as the comparison metrics for achieved Pareto sets under every experiment problem. Then, the outputs are indicated in Tables 7–10.

Fig. 9 indicates an instance of non-dominated solutions of proposed metaheuristic algorithms in the experimental problems e.g., SP8 and LP4. In these figures, HWOSA represents the worst efficiency while HSEO-FFA has mostly overcome the other metaheuristics. The solutions of other metaheuristics are same and close to each other.

Therefore, this paper performs a set of statistical comparisons between algorithms according to the Pareto optimal analyses by assessment metrics. Thus, the outcomes were presented in Tables 6–9 are converted to a famous criterion called Relative Deviation Index (RDI) in Eq. (57) (Goodarzian et al., 2020b; Goodarzian et al., 2021e). It is clear that a lower value of *RDI* obtains a higher quality of methods.

$$RDI = \frac{|Alg_{sol} - Best_{sol}|}{Max_{sol} - Min_{sol}} \times 100 \tag{57}$$

Table 7
NPS's computational outputs of the proposed algorithms.

Experiment problem	SEO	HWOSA	IKH	ISSO	HFFA-SA	HSEO-FFA
SP1	5	4	6	7	8	9
SP2	6	5	7	8	9	10
SP3	8	7	8	9	10	12
SP4	8	7	9	11	12	14
SP5	9	8	10	11	12	14
SP6	9	7	8	10	12	15
SP7	10	9	8	10	11	13
SP8	7	6	7	8	14	15
SP9	8	6	8	9	10	13
SP10	9	7	7	8	9	13
LP1	7	6	8	9	10	12
LP2	8	7	9	10	11	12
LP3	10	9	10	11	12	14
LP4	9	7	10	11	12	14
LP5	9	8	9	10	11	14
LP6	11	10	12	13	15	16
LP7	12	11	13	14	15	16
LP8	10	9	11	12	13	15
LP9	11	10	12	13	14	15
LP10	9	8	9	11	12	13

where $Best_{sol}$ shows the best solution between algorithms, Alg_{sol} indicates the value of obtained objective by an assessment metric of the method, and Min_{sol} and Max_{sol} define the minimum and the maximum values between all outputted values by methods.

In this regard, the means plot and Least Significant Difference (LSD) for the suggested methods is provided, while the outcomes run by Minitab 20. 1 Software are indicated in Fig. 10. According to Fig. 10, the HSEO-FFA algorithm has a robust performance than the other algorithms, but the HWOSA has a worst efficiency than the other methods.

6.3. *Sensitivity analyses for the proposed GMSCN problem*

To evaluate the model and analyze the effect of the parameters on the decision variables and the objective function value, a series of sensitivity analyses is hereby performed. Following is a description of the main parameters of the model and its effect on the model. In this part, a series of analyses of the problem to address the effectiveness of the model is performed. In the comparison section, the HSEO-FFA algorithm is used as an effective method for the sensitivity analysis. The objective function of the total cost with *TC* and environmental impacts with *EI* are shown. A small size experimental problem such as *SP4* is shown. To examine the model, only two parameters, namely tariff cost L_m^t, and the number of

Table 8
MID's computational outputs of the proposed algorithms.

Experiment problem	SEO	HWOSA	IKH	ISSO	HFFA-SA	HSEO-FFA
SP1	10.4322	12.3522	7.61822	5.44278	4.87322	4.33766
SP2	11.5611	14.5441	8.28228	6.88182	5.33708	4.88233
SP3	12.3219	16.1876	9.4451	7.2334	6.211	5.678
SP4	13.2332	18.2453	9.2145	8.2109	7.322	5.456
SP5	14.877	19.2763	10.8234	8.5231	7.566	6.321
SP6	16.032	20.344	12.2308	9.921	8.321	6.234
SP7	18.321	23.312	13.162	9.1430	9.675	7.345
SP8	20.455	26.344	14.289	10.1245	9.301	7.455
SP9	22.024	29.034	16.344	13.843	10.17	7.221
SP10	24.212	31.451	18.087	15.734	11.98	8.277
LP1	25.665	34.788	19.344	18.322	13.78	8.235
LP2	28.82	38.126	21.214	19.076	14.33	8.344
LP3	29.613	41.725	22.656	20.231	17.34	9.445
LP4	30.367	45.259	24.921	22.412	19.445	9.781
LP5	32.322	47.343	25.368	24.589	20.18	9.567
LP6	35.677	48.122	26.122	26.512	22.27	10.34
LP7	38.21	49.343	27.566	28.033	24.87	12.56
LP8	40.086	52.211	29.344	30.12	26.21	15.78
LP9	42.566	57.908	31.221	34.512	28.32	17.78
LP10	45.315	59.291	34.455	36.269	30.04	18.56

Table 9
MS's computational outputs of the proposed algorithms.

Experiment problem	SEO	HWOSA	IKH	ISSO	HFFA-SA	HSEO-FFA
SP1	4,765,122	4,566,781	4,877,134	5,186,344	5,455,423	6,784,123
SP2	4,890,344	4,788,908	5,184,551	5,788,629	6,133,776	7,853,362
SP3	5,165,532	4,907,881	5,344,721	5,988,212	6,562,321	9,850,532
SP4	5,498,071	5,123,345	6,712,351	6,885,329	8,776,423	10,348,256
SP5	6,147,665	5,344,561	8,789,234	7,871,321	10,556,698	15,677,701
SP6	6,677,832	5,677,801	9,852,425	9,455,421	13,647,799	20,358,819
SP7	7,489,063	6,123,348	10,445,541	11,248,343	18,843,441	28,682,321
SP8	8,165,321	6,344,567	12,356,221	16,122,543	22,678,418	32,888,326
SP9	8,765,432	6,889,024	14,634,879	18,265,581	28,709,321	40,883,260
SP10	9,187,321	7,345,677	16,513,291	23,566,712	34,467,711	45,670,721
LP1	9,521,894	7,665,671	18,744,297	28,703,441	37,045,633	49,830,432
LP2	9,878,341	8,034,456	25,674,982	33,520,289	36,785,231	51,783,447
LP3	11,780,322	8,456,671	27,803,412	36,775,221	42,334,351	56,791,038
LP4	14,804,328	8,809,561	29,833,831	38,989,812	45,633,233	58,361,326
LP5	19,260,981	9,265,432	32,949,524	42,368,923	46,932,808	60,945,233
LP6	21,561,081	9,566,781	34,566,129	44,566,709	50,123,447	63,445,501
LP7	26,875,132	9,806,671	37,899,012	48,023,445	53,445,501	67,889,120
LP8	29,985,421	10,456,731	40,123,357	51,344,290	55,677,891	72,334,501
LP9	32,376,109	13,455,621	42,344,566	53,445,987	58,993,421	79,023,411
LP10	37,504,451	15,667,832	45,677,021	59,880,761	61,233,406	83,445,602

Table 10
SNS's computational outputs of the proposed algorithms.

Experiment problem	SEO	HWOSA	IKH	ISSO	HFFA-SA	HSEO-FFA
SP1	695,631	655,467	786654.1	837556.1	8,846,345	956512.5
SP2	738,721	690,982	877,660	890927.2	901,856	1,031,212
SP3	804,332	756,221	901233.4	926276.8	917524.4	1,758,445
SP4	843,109	801,233	867719.3	961544.2	1,322,606	2,336,454
SP5	875,792	867,701	888253.2	991532.7	1,820,349	2,705,455
SP6	912,541	902,344	1,034,476	1137469.3	1,927,563	3,103,948
SP7	985,023	945,671	128167.8	1,138,936	2,354,672	3,696,782
SP8	1,094,332	997,560	132025.4	1,203,351	2,993,141	3,878,457
SP9	1,294,321	1,345,032	167515.6	2,349,402	3,418,719	4,546,711
SP10	1,894,309	1,677,899	2,377,872	2,856,234	3,787,360	5,255,282
LP1	1,906,768	1,906,788	2,834,136	3,454,742	3,967,352	5,945,512
LP2	2,532,102	2,345,576	3,227,661	4,179,224	4,244,557	6,412,893
LP3	3,198,328	2,908,768	3,427,883	4,454,456	4,641,788	6,934,233
LP4	3,798,125	3,245,556	4,543,427	4,989,214	4,917,345	7,233,712
LP5	4,134,268	3,677,840	4,772,311	5,189,231	5,155,905	7,529,322
LP6	4,589,543	3,908,762	5,123,445	5,567,789	5,356,678	7,809,912
LP7	5,067,825	4,355,617	5,344,781	5,890,811	5,908,712	8,012,334
LP8	5,283,357	4,890,129	5,889,021	6,234,419	6,234,789	8,345,512
LP9	5,793,289	5,012,349	6,233,091	6,790,871	6,987,701	8,677,981
LP10	6,209,549	5,890,917	6,782,331	7,012,364	7,235,518	9,012,344

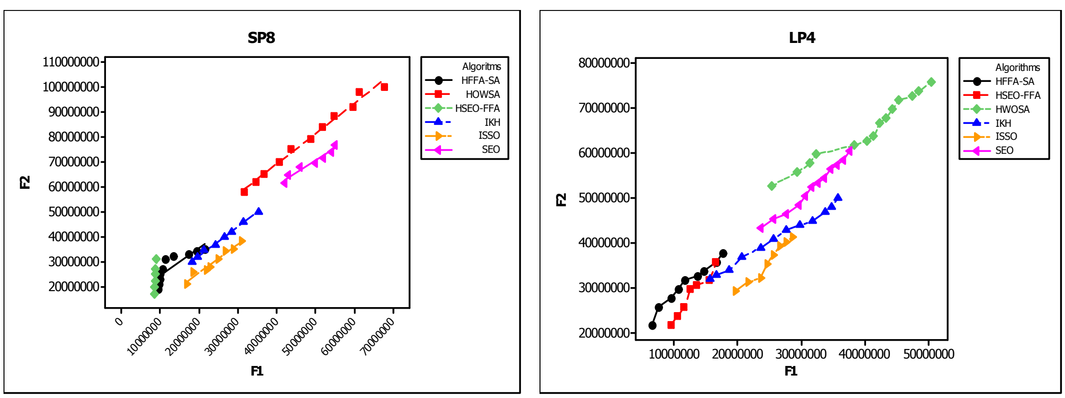

Fig. 9. Pareto frontier of algorithms in the *SP*8& *LP*4 samples.

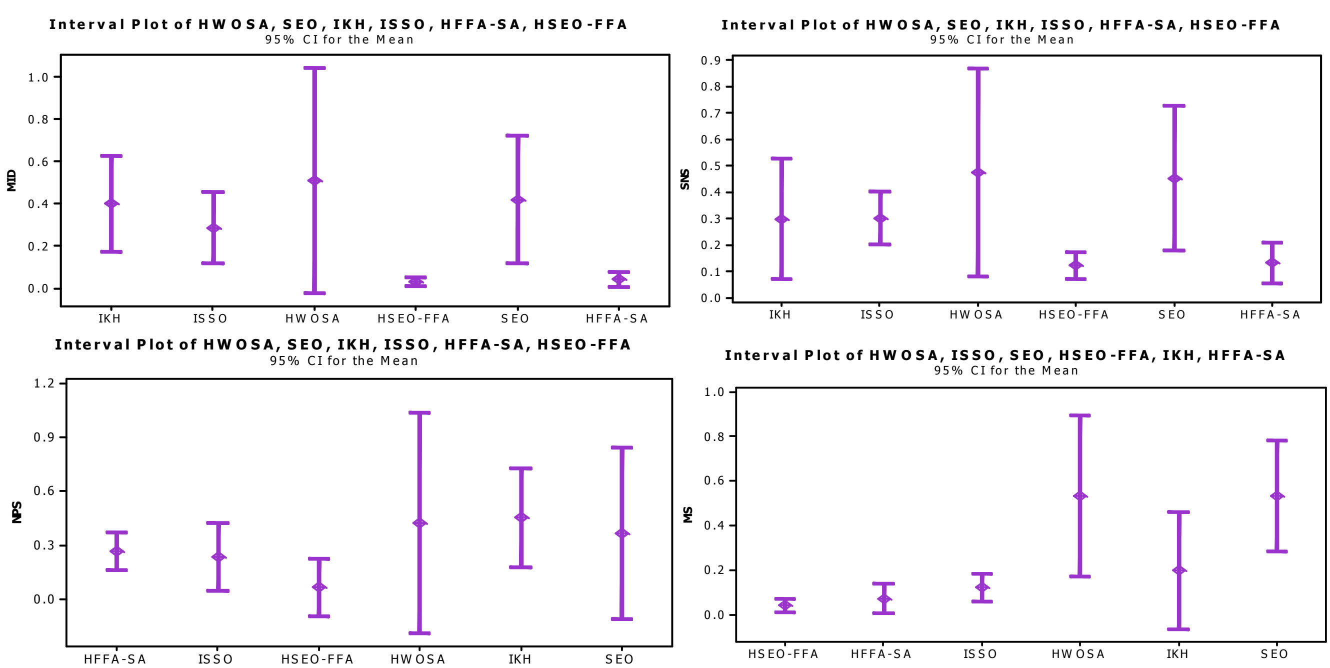

Fig. 10. ANOVA plots for the evaluation metrics in term of RDI for the proposed methods.

Table 11
The sensitivity analysis outcomes relevant to the tariff cost.

No. instances	L_m^t	*TC*	*EI*
C1	300,000	5122341.4	9865543.14
C2	400,000	5587122.35	10431348.39
C3	500,000	5937577.21	12856670.17
C4	600,000	6235788.45	14557871.23
C5	700,000	6551232.78	18821128.76

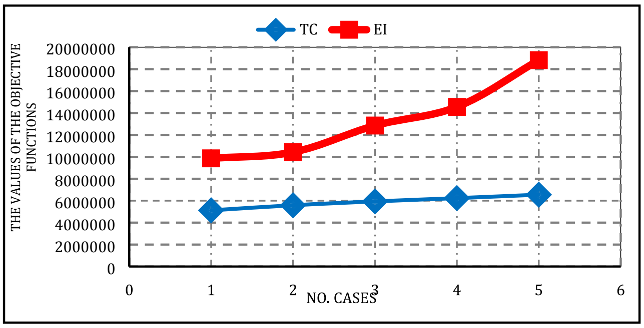

Fig. 11. Objective functions behavior for sensitivity analysis based on the tariff cost.

Table 12
The sensitivity analysis outcomes relevant to the sorts of transportation systems.

No. instances	*#v#k*	*TC*	*EI*
C1	#3#6	5122341.4	9865543.14
C2	#4#7	5456111.57	12356612.23
C3	#5#8	6223628.88	16782272.73
C4	#6#9	6567449.07	21337122.07
C5	#7#10	6984412.12	26677031.19

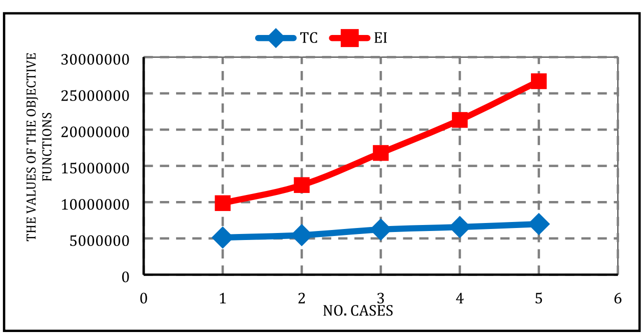

Fig. 12. Objective functions behavior for sensitivity analysis based on the sorts of vehicles.

sorts vehicle v and k are examined in this section. Therefore, five experiments for each parameter are designed and changed related to the objective functions. The applied sensitivity analysis of this parameter and the relevant results are presented in the Table 11. Besides, the trade-off among objective functions including the environmental impacts and total cost are provided as the values of normalized in Fig. 11. The results show a stunning similarity between the objective functions. In overall, with the increase in tariff costs, not only does the total cost of medicines increase, but also the environmental impacts of vehicles and inter-network routes heightens.

In general, the most important contribution of the suggested bi-objective model is to consider different multi-modal transportation. In this regard, sensitivity analysis has been carried out with an increasing variety of transportation systems to evaluate its effect on the target functions. Table 12 illustrates the results of this paper and Fig. 12 shows the behavior of the objective functions, based on the types of the transportation systems.

The results show a contradiction between the objective functions. Although environmental impacts intensify as the number of vehicles raises, the total cost is remained constant. With an overview, choosing the best strategy for deploying the most efficient transport systems can be very useful in responding to the concerns about the cost of transportation.

6.4. Managerial implications

According to the GMSCN, the IPCs, FPCs, pharmacy and hospital can decide the ordering policy, distribution of medical products, and also the sort of vehicle for transportation of medical products that best suits them. Results indicate that the developed model is robust through the GMSCN size (i.e., number of pharmacies and hospitals in the GMSCN, the number of transportation systems, the number of IPCs, and FPCs, and the number of medical products). Therefore, the developed model can be utilized for developing policies for both DCs of medical products. In case if the hospitals and pharmacies, and IPCs and FPCs are experiencing high demand variability, it is strongly recommended to utilize the HSEO-FFA metaheuristic algorithm. Likewise, when transportation costs by using different vehicles are significantly higher or lower than the setting considered in the present paper, so it is efficient to utilize the HSEO-FFA algorithm. On the other hand, the DC capacity constraints applied to efficiently holding of medical products from the IPCs and FPCs to various pharmacies and hospitals as well as control of other decisions made in the inventory and distribution system are significant. For example, if a major number of medical products arriving at a hospital and pharmacies are old and have only an expiry date by one day, the hospitals and pharmacies will experience more wastage, and the hospitals and pharmacies will likely place more purchase orders to pay damages for the outdating. A rise in pharmaceutical product purchase may lead to a shortage at the DCs, which in turn may lead to an increase in emergency transportation by using a plane vehicle from other DCs. Based on this allocation and distribution constraints will be affected by the number of hospitals, pharmacies, and DCs.

7. Conclusions and future works

In this paper, a new MILP model was extended for optimizing environmental and economic impacts objectives, which both aims involve decreasing inventory holding costs, fixed costs for IPC, FPC, and the establishment of pharmacy and hospital, transportation costs, establishing and packing costs, and purchasing costs and minimizing the amount of released CO_2 emission by transportation systems and establishing pharmacy and hospitals. Then, a new multi-period, three-echelon, multi-product, and bi-objective Green Medicine Supply Chain Network is proposed along with the environmental impacts under uncertainty with multi-modal transportation. Hence, one of the significant contributions of this paper is related to the environmental impacts in the whole GMSCN associate with the establishment of pharmacies and hospitals and the green effect related to the released carbon dioxide (CO_2) by transport vehicles. Furthermore, the GMSCN model and a fuzzy programming were developed to examine the effects of uncertain parameters, containing uncertainty on transportation and inventory holding costs. This wide implementation of uncertain parameters in the proposed model causes it more realistic and closer to the real-world practice. However, methods to tackle with uncertain parameters differ in the scope and nature of the papers. In real case studies, to comment on how performance each of these techniques may be, one needs to compare them that can be offered as one idea for the interested scholars in the future works. In terms of solution methodology, due to the complexity of the GMSCN model and NP-hard, we have developed two new hybrid metaheuristic algorithms include HSEO-FFA and HFFA-SA algorithms to achieve Pareto optimal solutions for the GMSCN problem. Therefore, we provided these algorithms to solve the optimization problems in optimal and near-optimal spaces. In order to validate the model, some numerical examples in different sizes include small-sized and large-sized problems are tested into the proposed platform. Then, the obtained results based on the objectives and required CPU time are compared on the different scales. Moreover, the CPLEX solver is used in small-sized problems to crack the problem. In the next part, the suitable sensitivity analysis of the main parameters are catered to test the validation of the obtained results. After that, four assessment metrics include NPS, MID, MS, and SNS are offered to analyze the presented metaheuristic algorithms in different size problems. As a result, the CPLEX method is better than other suggested methods in small-sized problems. However, the HSEO-FFA algorithm is more robust, swifter and more efficient than other proposed algorithms in different sizes. It is clear that the HSEO-FFA algorithm had a high quality, the best performance, and high convergence than other the proposed algorithms according to the four-assessment metrics and CPU time. Moreover, HSEO-FFA has been indicated a minimum average of CPU time (1913.408 s) but HWOSA has been shown the maximum rate of this item (3256.667 s).

In future works, interested researchers can use robust or stochastic approaches to cope with the input parameters that have stochastic nature, including costs, capacity, demand, and transportation system. On the other hand, the objective functions include maximizing customer satisfaction and minimizing the unmet demand for medical products can add to our model objective functions. Additionally, some resilience measures can be incorporated in order to elevate the performance of the model under extreme events. The interested scholars could utilize other metaheuristic and heuristic algorithms and compare them with the results of our model in order to solve the model.

Then, similar to the other studies, the current paper has a few limitations as follows:

- One of the limitations of the research is the lack of access to accurate information about transportation costs and the selection of the types of vehicles. Moreover, in this study, only the information of the drivers and experts about transportation costs and the selection of the types of vehicles have been sufficient.
- One of the important and significant limitations in this paper, the lack of benchmark functions and inaccessibility of real data. Because of this, several test problems with simulated data in different sizes are designed to validate the proposed model.
- In order to implement meta-heuristic algorithms, high RAM and CPU hardware features and software features such as MATLAB software are needed.

CRediT authorship contribution statement

Fariba Goodarzian: Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Samuel Fosso Wamba:** Resources. **K. Mathiyazhagan:** Visualization. **Atour Taghipour:** Supervision, Validation, Project administration, Review & editing.

Declaration of Competing Interest

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

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