

Designing a Decision Support System for Estimating the Retailer's Demand for Cancer Drugs

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Abstract

Cancer drugs and the process of manufacturing these drugs are complicated and costly. In addition, these drugs are among the vital drugs, hence the necessity for their availability to patients. Therefore, we decided to create a decision support system that estimates the number of cancer drugs needed for patients during certain periods by minimizing the marginal cost. This decision support system is appropriate for predicting, not making decisions instead of humans. We illustrated its pharmaceutical supply chain and we modeled the problem as a mathematical model to solve this problem. The innovation of this article is to create a decision model for a pharmaceutical supply chain that can be the basis for creating a decision support system. Also, this flexible supply chain can be changed according to the user's needs. Finally, we solved the problem in Excel using the Solver library. This decision support system gets the values of the

indices from the user and creates a supply chain in proportion to the user's need. Data provided by Alborz Pharmed Company was used to test this decision support system. The model results revealed the strategic and management decisions made in the distribution network of Regorafenib in Tehran.

Keywords: pharmaceutical supply chain, cancer pharmaceutical manufacturing, linear programming, distribution network, supply chain decision support system

Introduction

Since cancer is currently considered one of the major and costly diseases in society, authorities have to take into consideration the timely supply of drugs at the lowest cost to the patients. The prime cost of drugs should not increase due to reasons such as the shortage of drugs, long-term storage of drugs or unnecessary storage of drugs, involvement of many middlemen, and unbalanced drug distribution (i.e. fewer drugs are provided to regions that demand more cancer drugs and more drugs are provided to regions that demand fewer cancer drugs) [3].

Since the increased industrialization of drug production, information technology has always assisted this industry. In recent years, many techniques of the advanced industries

have been employed in combination with the information technology in the pharmaceutical industry. Hence, the technologies of advanced industries have found their way into the pharmaceutical industry [14, 13].

The pharmaceutical supply chain calls for more attention than the other industries due to the dire need of patients for drugs [5]. The constant flow of drugs to the patients has to be ensured in the pharmaceutical supply chain. This flow has to continue at the optimal price and drugs have to be delivered to the patients with minimum delay. Moreover, patients should not suffer from the shortage of drugs [6]. Over the past several years, pharmaceutical industries have realized that they should produce drugs in proportion to the demand instead of the mass production of drugs to prevent the loss of drugs. The number of drugs produced also has to be changeable [14, 13]. Since perhaps there is a shortage of resources for drug production, the number of drugs produced should match the demand. Sometimes the shortage of resources does not occur in the beginning because it occurs as a result of a state of emergency [14].

Drugs are among the important and special commodities consumed by patients. If the production of drugs does not match the number of patients, patients will face difficulties. Hence, drug production has to match the demand [15]. In the previous research, a drug distribution method is introduced based on a mathematical model. In this method, all the variables are obtained. Thereafter, the problem objective equation is written and it is solved based on an artificial intelligence algorithm [4]. The pharmaceutical supply chain management

methods are also discussed [13]. Another method is also introduced. This method uses the linear regression and genetic programming techniques to forecast the market demand for drugs and its actual consequences are discussed [7]. Therefore, the study problem is the problem of supplying cancer drugs in proportion to the market demand and minimizing the supply chain costs. The reason for solving this problem is the failure to produce cancer drugs based on accurate statistics on the market demand.

In this study, we tried to develop a decision support system that forecasts market demand. This decision support system receives values from the user and creates the supply chain for the user. This system is fully described in the following sections. The difference between the methods proposed in this study and the previous studies lies in the creation of a flexible supply chain based on the values provided by the user. Moreover, the primary suppliers or producers of drugs are added to this supply chain.

The Supply Chain Structure

Generally, every pharmaceutical company in every county has to identify its pharmaceutical supply chain to improve its production process [13]. Asamoah et al. (2012) fully studied the pharmaceutical industry and suggested that a hierarchical chain approach to the pharmaceutical companies has to be taken. They studied this suggestion by analyzing antimalarial medications [2]. Yu et al. (2010) indicated that every pharmaceutical supply chain consists of four parts: 1) the drug producer, 2) the drug distributor, and 3) the drug retailer (including hospitals, pharmacies, and clinics) [15].

However, there are factories that produce the raw materials for the production of drugs. This form of raw material production is called primary production of drugs, while the production of the drug and packaging are considered secondary production [16]. The pharmaceutical supply chain networks can have several products and periods. They can also include several primary and secondary production centers. In this supply chain, the production centers are followed by the

distributors and retailers (i.e. the hospitals, clinics, and pharmacies) [13]. In 2012, Mehralian et al. introduced a form of the pharmaceutical supply chain blocks, which included the drug producer, the drug distributor, the drug retailer, and the patients [15]. Our goal is to complete this diagram and add the primary drug producer or the supplier to the diagram (Figure 1).

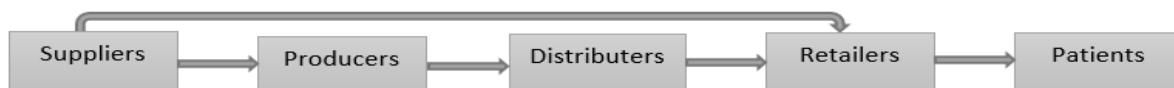


Figure (1) Components of the pharmaceutical supply chain

Designing the Cancer Drugs Distribution Network

Mousazadeh et al. (2015) proposed a diagram of the pharmaceutical supply chain network, which included the distributors and retailers. Our goal is to approach

this supply chain from a novel point of view and illustrate this network with the primary producer, i.e. the supplier [12](Figure 2).

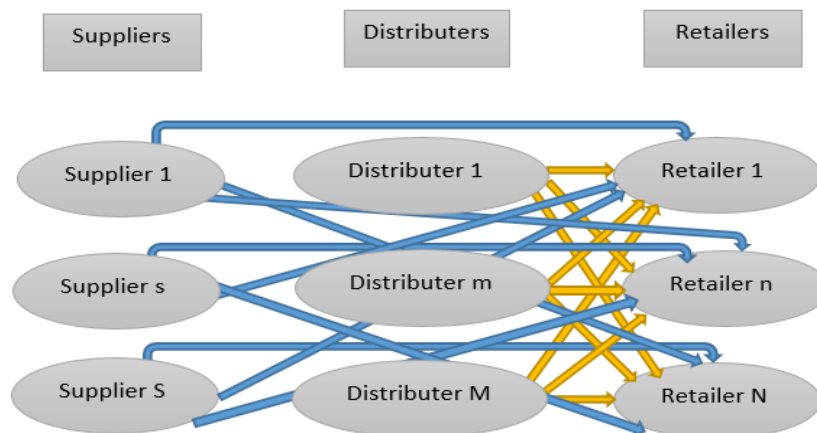


Figure (2) Pharmaceutical supply chain distribution network

The decision problem here is the design of a system for contributing to the estimation of the number of cancer drugs needed for hospitals, pharmacies, and cancer treatment centers. The reasons for selecting this problem are: 1) cancer drugs are very expensive and their production and distribution have to be carried out based on accurate statistics at customers' request; 2) cancer drugs have very strict storage requirements and their production should not exceed the customer demand to prevent the loss of drugs; 3) production of cancer drugs is a complicated time-consuming process and thus their production should not exceed the market demand.

This problem was modeled using the mathematical modeling method. Mathematical modeling is one of the fundamental concepts in operations research. Since

a system has to be first defined in mathematical terms to be analyzed, the first step after identifying the target system is turning it into a mathematical model. In other words, an index, a parameter, and a decision variable are defined based on the problem model. Mathematical models have an objective. Here, the goal is to reduce the operating costs. The formula for the problem objective function is also identified using a combination of the index (Table 1), the parameter (Table 2), and the decision variable (Table 3). Finally, the problem constraints are formulated. These models are inspired by three models: Mota et al. (2012) [8]; Mousazadeh et al. (2015) [9]; and Nasibeh Janatian et al. (2018) [7].

Table 1- The indices of the pharmaceutical supply chain

Products	I
Raw materials	J
Producers	K
Suppliers	S
Distributers	M
Retailers	N
Transportation vehicles set	G

Monetary units set	U
Supplier states set	C
Period	T

Table 2- The parameters of the pharmaceutical supply chain

The number of demands for each product per retailer	d_{in}
Capacity per producer	h_k
The number of consumption of each raw material type per unit of each product type	S_{ij}
The cost of buying each raw material type per supplier	W_{js}
The cost of producing one unit of each product type per producer	L_{ik}
The cost of storing one unit of each product type per distributor	r_{im}
Fixed cost of employing each producer	f_k
Fixed cost of employing each distributor	f_m
A large constant	P
The cost of transfer of the raw material per unit between the supplier and producer	tl_{jsk}

The cost of transfer of each product type per unit from each producer to each distributor	t_{ikm}^2
The cost of transfer of each product type per unit from each distributor to each retailer	t_{imn}^3
The cost of transfer of each product type per unit from each supplier to each retailer	t_{isn}^4
The border tax for shipment from one county to another per unit of the each raw material type	T_{jcu}
Weight displaceable by each vehicle	w_g
The number of currency available for importing	y_i
The cost of storing one unit of each product in the central warehouse	t_{cwi}

Table 3- The pharmaceutical supply chain decision variables

The number of raw materials sent by each supplier to each producer within period t	V_{jskt}
The number of each product type produced per producer	Q_{ik}
The number of products of each type sent by each producer to each distributor within period t	Y_{ikmt}

The number of products of each type sent by each distributor to each retailer within period t	X_{imnt}
The number of products of each type sent by each supplier to each retailer within period t	Z_{isnt}
Employing a producer: 1 if employed; otherwise 0.	W_k
Employing a distributor: 1 if employed; otherwise 0.	U_m
Suppliers: 1 if it is in another country; otherwise 0	L_s
If we have a central warehouse within period t: 1 if yes and 0 if no.	Cw_t

Mathematical Model

1) The cost of buying and transporting raw materials

Min w1=

$$\sum_{j=1}^J \sum_{k=1}^K \sum_{s=1}^S \sum_{c=1}^C \sum_{u=1}^U \sum_{t=1}^T (W_{js} + t_{1jks} + T_{jcu}) * V_{jskt}$$

2) Production cost

Min w2=

$$\sum_{k=1}^K \sum_{i=1}^I L_{ik} * Q_{ik}$$

3) Cost of shipment from the producers to distributors

Min w3=

$$\sum_{i=1}^I \sum_{k=1}^K \sum_{m=1}^M \sum_{t=1}^T t_{2ikm} * Y_{ikmt}$$

4) Cost of shipment from distributors to retailers

Min w4=

$$\sum_{i=1}^I \sum_{n=1}^N \sum_{m=1}^M \sum_{t=1}^T (r_{im} + t_{3imn}) * X_{imnt}$$

5) Cost of direct shipment from the suppliers to retailers

Min w5=

$$\sum_{i=1}^I \sum_{s=1}^S \sum_{m=1}^M \sum_{t=1}^T (t4isn + (Cwt*tcwi))*Zismt$$

6) Fixed cost of employing producers

Min w6=

$$\sum_{k=1}^K fk*wk$$

7) Fixed cost of employing distributors

Min w7=

$$\sum_{m=1}^M fm*Um$$

8) The aggregate objective function of the 7 functions introduced above is

Min wt=

$$w1 + w2 + w3 + w4 + w5 + w6 + w7$$

9) First constraint: The number of each product type received by each retailer shall not exceed the demand for that product.

$$\sum_{i=1}^I \sum_{n=1}^N \sum_{m=1}^M \sum_{t=1}^T Ximnt \leq din, \forall i, n$$

10) Second constraint: The number of each product type shipped by each producer

shall not exceed the production of that product.

$$\sum_{i=1}^I \sum_{k=1}^K \sum_{m=1}^M \sum_{t=1}^T Yikmt \leq Qik, \forall i, k$$

11) Third constraint: The raw materials used by each producer shall not exceed the raw materials sent by the suppliers.

$$\sum_{i=1}^I \sum_{k=1}^K \sum_{j=1}^J Sij*Qik \leq \sum_{i=1}^I \sum_{k=1}^K \sum_{s=1}^S \sum_{t=1}^T Vjskt$$

12) Fourth constraint: The number of products sent by each distributor to each retailer shall not exceed a number determined by the user if a distributor is employed

$$\sum_{i=1}^I \sum_{n=1}^N \sum_{m=1}^M \sum_{t=1}^T Ximnt \leq P*Um, \forall m$$

13) Sixth constraint: Variables used to employ the producer and the distributor are either 0 or 1.

$$Wk, Um \in \{0, 1\}, \forall k, m$$

14) Seventh constraint: The number of raw materials sent by each supplier to each producer within period t, the number of products of each type produced by each producer, the number of products of each type sent by each producer to each distributor within period t, the number of products of each type sent by each distributor to each retailer within period t, and the number of products of each type sent by each supplier to

each retailer within period t are the values that have to be greater than or equal to zero.

$$V_{jskt}, Q_{ik}, Y_{ikmt}, X_{imnt}, Z_{isnt} \geq 0 \quad (14)$$

The Problem Solving Approach

The mathematical problem above modeled the pharmaceutical supply chain of the cancer drugs supply chain. The aggregate function introduced in no. 8 has to be minimized to minimize the overall cost of this supply chain.

This problem is solved in Excel using the Visual Basic macro codes and Solver library. Solver uses GRG nonlinear algorithm for

solving problems. In step one, we create a user environment. In this user environment, first, we place all parameters in a row on the plane by alternately creating the columns. The columns are created alternately to enable the user to write the values of the parameters in front of them. We do the same for the decision variables to enable the user to see the decision variable values after solving the problem. Thereafter, the problem is solved using the SolverOK and SolverAdd functions of the Solver library. Function “SolverOK” is used to identify the objective function and maximize or minimize this function (Figure 3).

```
SolverOK SetCell:=Range("CV6"), _
    MaxMinVal:=2, _
    ByChange:=Union(Range("BC9:BC" & (Row - 1)), Range("BE9:
```

Figure (3) Calling SolverOK for solving the problem

SetCell determines the final objective function cell. If MaxMinVal is 2, the objective function is minimized. Besides, ByChange determines the decision variables

cells. The SolverAdd function also identifies the problem constraints (Figure 4).

```
SolverAdd cellRef:=Range("BZ" & Index), _
    relation:=1, _
    formulaText:=Range("CD" & Index).Value
```

Figure (4) Calling SolverAdd for solving the problem

The values in the constraint columns are written on the two sides of this function, and “relation” shows the relationship between these two columns. If this number is 1, the left side is greater than or equal to the right side. If this number is 2, the left side is smaller than or equal to the right side. This function is called for each constraint. This method enables the user to create a desired supply chain and solve the problem by

initializing the parameters. In addition, the user can exactly determine the final objective function value.

Empirical Study

The supply chain selected for testing the proposed solution is the supply chain of an Iranian company named Alborz Pharmed Company. This company is a powerful

company in the production of different types of drugs. We selected Regorafenib drug, which is produced by this company, to test the solution. “Regorafenib” is important for the treatment of colon, stomach, and liver cancer patients. This drug is among the very expensive drugs.

Three types of main raw materials are purchased from other suppliers for the production of this drug. There are two main suppliers that supply these necessary raw materials. We want to regulate the distribution of this drug in Tehran City based on the market demand. Alborz Pharmed has three primary distributors in Tehran Province for the distribution of this drug. Besides, the

retailers selling this drug in Tehran Province are classified into 5 groups. In Tehran Province, 4 vehicles are allocated to the transfer of this drug. The monetary units include toman and euro. Germany is also the supplier of this drug. A short time period consisting of three months is selected due to the currency changes in Iran and the increased supervision over the supply of this type of drug. Considering the discussion above, the problem indices are listed in the following table (Table 4).

Table 4-The empirical research indices

I=1	Products	i
J=3	Raw materials	j
K=1	Producer	k
S=2	Producer	s
M=3	Distributor	m
N=5	Retailer	n
G=4	Vehicles set	g
U=2	Monetary units set	u
C=2	Supplier countries set	c
T=3	Period	t

The data needed to solve the supply chain problem has been obtained from Alborz Pharmed Company. Thereafter, the solution to this problem reveals the number of raw materials that has to be sent by the supplier to

Alborz Pharmed. It also determines the number of Regorafenib drugs that have to be produced in Tehran, the number of each drug that has to be received by the distributors in

Tehran, the number of each drug that has to be delivered to the

retailers in Tehran, and the number of drugs that have to be directly sent from the suppliers to the retailers in Tehran. In the following tables the values of the number of Regorafenib drugs sent to the distributor

(Table 5), the number of Regorafenib drugs sent from the distributor to the retailer (Table 6) and the number of Regorafenib drugs sent from the supplier to the distributor (Table 7) are written.

Table 5-The number of Regorafenib drugs sent to the distributor

Distributor	The number of Regorafenib drugs sent to the distributor
Distributor 1	210
Distributor 2	451
Distributor 3	226

Table 6-The number of Regorafenib drugs sent from the distributor to the retailer

Distributor	Retailer	The number of Regorafenib drugs sent from the distributor to the retailer
Distributor 1	Retailer 1	0
Distributor 1	Retailer 2	92
Distributor 1	Retailer 3	54
Distributor 1	Retailer 4	0
Distributor 1	retailer 5	64
Distributor 2	Retailer 1	85

Distributor 2	Retailer 2	151
Distributor 2	Retailer 3	0
Distributor 2	Retailer 4	107
Distributor 2	Retailer 5	108
Distributor 3	Retailer 1	53
Distributor 3	Retailer 2	69
Distributor 3	Retailer 3	55
Distributor 3	Retailer 4	48
Distributor 3	Retailer 5	0

Table 7-The number of Regorafenib drugs sent from the supplier to the distributor

Distributor	Retailer	The number of Regorafenib drugs sent from the supplier to the retailer
Supplier 1	Retailer 1	106
Supplier 1	Retailer 2	0
Supplier 1	Retailer 3	0
Supplier 1	retailer 4	110
Supplier 1	Retailer 5	90
Supplier 2	Retailer 1	0
Supplier 2	Retailer 2	60

Supplier 2	Retailer 3	98
Supplier 2	Retailer 4	0
Supplier 2	Retailer 5	0

Conclusion

Today, the expenses of pharmaceutical companies producing cancer drugs are high. Besides, patients buying these drugs are in a very critical condition and need to access the drugs. Given the heavy costs of cancer drugs, extra costs should be avoided and the marginal cost has to be minimized. Based on these requirements, we developed a decision support system that is capable of estimating the market demand by minimizing the costs. The solution to this problem provides an estimation of the number of drugs that have to be produced. It also determines the number of drugs that have to be delivered to each distributor following production, the number of raw materials needed to produce the required number of drugs, and the number of drugs that are delivered to the distributors and have to be delivered to the retailers subsequently. For instance, 887 boxes of Regorafenib have to be produced within 3 months in Tehran City, and 451 boxes have to be delivered to the second distributor. The second distributor has to deliver 107 boxes to the retailer. Moreover, the first supplier directly delivers 110 boxes of this drug to the fourth retailer. To produce this number of drugs, 280 kilograms and 120 kilograms of the first raw material are sent by the first and second suppliers to the producer, respectively. Moreover, 400 kilograms and 100 kilograms of the second raw material are sent from the first and the second supplier to

the producer, respectively. Besides, 250 kilograms and 400 kilograms of the third raw material are sent from the first and second suppliers to the producer, respectively.

This decision support system is developed using Solver library in Excel. One of the challenges to the development of this decision support system is that if the number of parameters, decision variables, and constraints exceeds a certain limit, the commercial version of Solver has to be purchased. Therefore, the commercial Solver version is needed to improve the solution to the problem. We requested the required data from Alborz Pharmed Company. Besides, only one of the cancer drug products of this company is selected to provide a more clear explanation of the results of this study. Therefore, more products can be added to this problem. We suggested the proposed solution to Alborz Pharmad. Based on the fact that the time period is 3 months and there is no change in the values of the indexes and parameters, we suggested them to try the solution. For the next 3 months, they produced as much as we said and distributed to distributors as much as we said. Their final response was positive, and they said the solution worked for us. For the next three months, they produced as much as we said and distributed to distribution centers as much as we said. Their final response was positive, and they said the solution worked for us. For further research, it is

recommended to combine this solution with machine learning to find a more flexible and robust solution. Moreover, this problem is solved as a static problem regardless of the three-month periods, while it can be solved as a dynamic problem and drugs with special storage requirements can be added to the problem space.

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