Journal of Quality Engineering and Production Optimization

Vol. 5, No. 2, Summer & Autumn 2020

http://jqepo.shahed.ac.ir

Research Paper

DOI: 10.22070/JQEPO.2021.5332.1145

System Dynamics Approach to Model the Interaction Between Production and Pricing Factors in Pharmaceutical Industry

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Abstract – *Pharmaceutical companies need to take advantage of adequate profits to obtain sufficient funds for playing major roles in the competitive market. The purpose of this research is to predict the price of medicine and the volume of production, taking the producer's profit, the prices of the raw materials, and qualities into consideration. System thinking is employed to develop the cause and effect diagram and system dynamics for preparing the model for simulation and trend analysis. The simulation was carried out using VENSIM software on the amoxicillin capsule as a case study. When the government increases the marginal profit percentage for producers and with high-quality raw materials used by the producer, the companies` profits, production volume, and medicine quality will increase. Sensitivity analysis indicates that our pharmaceutical production company can better deal with the pharmacies, producers, and suppliers. This means that with a two percent lower profit margin for the pharmacy industry, the final medicine price would come down to 40105 from 40601, which is a one percent reduction to the base price suggested by simulation originally. This article makes a significant contribution to the Pharmaceutical field and hence to the patients and health industry.*

Keywords– *Production, medicine Production, System Dynamics, Scenario making.*

I. INTRODUCTION

Medication is the most important and widely used health aid, which is complementary to the patients' treatment cycle where its vital role in human life is not surreptitious. There exist some steps that a single medicine takes toward the patients as medicine production, medicine distribution, physician prescription, and medicine consumption. Each of these steps can be considered as a system that is comprised of different subsystems. One of the most important of these four subsystems is the medicine production system; because the cost of medicine production determines the base price of a medicine, which has a significant effect on the behavior of other subsystems. Therefore, considering the importance of the medicines' base price in this study, the authors will consider the production costs and the factors that influence that.

In the field of pharmaceutical production, production costs increase due to the increase of R&D costs, raw materials costs, human resource expenses, equipment investments, and the application of new technologies, which is always in order. Technology and innovation are the main characteristics of this category, if it fails to keep pace with the requirements of this classification, it will fail to perform well, and the situation gets hard in providing the community

Manuscript Received:28- Sep -2020 & Revised:19- Oct -2020 & Accepted: 27- Dec -2020
ISSN: 2423-3781

with the right medicine at the right time, and with the right amount.

On the one hand, the production system faces high cost and consuming time in the production process because it takes at least 12 years to discover the formula and then develop a new medication, with an average cost of more than a billion dollars which is more than NASA's budget to send a rocket to the Moon (Zhao & Chen, 1990). This indicates the high cost of research and development. The share of R&D spending in Iran is very low, as compared with developed and developing countries, indicating the uncompetitive atmosphere of the Iranian economy and the lack of incentives for firms to invest in R&D activities (Amini & Zolfaghari, 2010). Nowadays, the high cost of medication production and its ongoing increase is a global concern. Competitiveness is considered one of the essential factors in developing industries, and the pharmaceutical industry is no exception (Gholamian et al., 2014). Considering the issues mentioned above, medication manufacturing must have the financial resources needed to survive in this industry and provide the conditions and incentives to innovate, increase productivity, and improve the medication's quality to keep the medication industry dynamic.

On the other hand, the rapid increase in medicinal costs and the need for health budget controls have fueled interest in renewing medication pricing policies (Levaggi, 2014). Increasing health care spending in most countries around the world has become a significant concern for health executives and policymakers. In addition to promoting the community's health, the community health system should also be responsible for protecting them against the financial costs of receiving health services. Medicare, counseling, and nursing costs account for the largest proportion of spending in the world health system, respectively. In recent decades, the growth rate of pharmaceutical spending has been much higher than the overall growth rate of health care spending. A study in Sweden found that between 1974 and 1995, medication costs based on the adjusted general inflation rate were increased by 133 percent. Also, in the Organization for Economic Cooperation and Development member countries between 1998 and 2007, the growth rate of pharmaceutical spending was equal to 50%. In the United States, pharmaceuticals' cost increased from 1.5 percent of total health spending in 1980 to 7.9 percent in 2000. Besides, it is expected that medication spending will continue to rise in the coming years and put a substantial strain on health care systems. In recent years, pharmaceutical spending has become a major concern for health policymakers worldwide, both in absolute terms and in terms of its share of total health spending (Levaggi, 2014).

Therefore, the management of medication production costs is of particular importance both for the boom in the pharmaceutical industries and for the efficiency of the health systems of each society. It examines the relationships between different parts of a system.

II. LITERATURE REVIEW

In the study of medication production, it has been pointed out that investment in pharmaceutical research and development requires sustained financial commitments and sustained investment in high medication prices, which is why medication developers are prone to prices. The current generation of medication relies on the support of the next generation of their products. The high prices of specialized medication reflect the costs of research, production, and distribution, and that a reliable pricing model can support medication development and discovery (Robinson & Howell, 2014).

A study conducted in South Korea pointed out that rising medication costs are linked to new medications and their marketing and price reductions. Also, pharmaceutical companies tend to execute marketing strategies when they gain profit per unit, thereby finding new markets (Cho et al., 2015). Highlighted cases in a review study of increased pharmaceutical costs associated with production include new medication, increased medication waste due to new drugs, increased access and use of generic medications (Mousnad et al., 2014).

In a study, medications should be classified by innovation. By defining a rational solution to rewarding true innovation for highly innovative medications with cost-effectiveness estimation, more innovative therapeutic outcomes can be achieved. Such a "Binary approach" limits the cost of pharmaceuticals and rewards companies at high risk of investing in basic research (Garattini et al., 2007).

A study in Malaysia noted that reducing the basic medication price (production costs) did not work to reduce people's medical costs and control medication distributor profits. It is necessary, as a decrease in the medication base price will mislead retailers and pharmacists and increase their profits without reducing public health costs (Babar et al., 2007).

A study in 2014 presented a model with a dynamic systems approach to explain the high cost of medicines for patients in Chinese hospitals. One of the reasons for the high cost of pharmaceuticals is the benefit that hospitals and doctors receive by prescribing expensive, unnecessary drugs. The unnecessary prescription will lead to an overdose of a medication, which concluded that the study should eliminate the link between medication sales profits and physician prescriptions and hospital revenues. To address these issues, suggestions have been made; Fundamental reform of the health system, reforming of the hospital operating mechanism, reforming the drug distribution system, and budget allocation for various departments should be considered (Li et al., 2014).

In a study, Abdollahi Asl and colleagues used a dynamic system approach and examined the national medical policy in Iran, including medication production. Production-related issues were addressed in this study included internal competition, cost of medication production, internal drug prices, quality, research and development, and producer profits (Abdollahiasl et al., 2014).

A study examined the process of targeting medicine subsidies in Iran during the years 1995-2003 and the efficiency changes in the pharmaceutical industry. In this regard, the developments of the country's pharmaceutical market and its more competitive with the increase of drug production in this sector were considered as an indicator for increasing the efficiency of the industry. The observations of this study suggested that increasing the efficiency of the country's pharmaceutical industry during these years had helped to make the country's pharmaceutical market competitive and increase medication production (Ebadi & Ghavam, 2009).

The cost of raw materials accounts for a significant portion of the cost of a medication, accounting for about 50% of the cost. Exchange rate changes can have a significant impact on the cost of purchasing imported raw materials. In Iran, about 70% of the raw materials needed for medication production are imported from outside of the country. Although the cost of wages is one of the most significant cost items in medication production (having the highest rank after raw materials), its share of the total cost of medication production is not significant but accounts for about 14% of the total cost. This may indicate that the drug manufacturing industry is more technology-based than the user industry and can, therefore, be expected to be highly sensitive to any policies that lead to higher technology prices (Kalantari et al., 2014).

The variables which affect the productivity of total factors of production are divided into three main categories: technical knowledge, human resources capital, and social capital. Its technical knowledge includes factors such as foreign technology transfer, business research, and development activities of ICT and ICT. Therefore, improving productivity is a prerequisite to maintain the competitiveness of firms. On the other hand, the lack of public attention to the brand name of domestic medicines has led to a high-profit margin for firms, which has limited the incentive to improve productivity in pharmaceutical companies (Amini & Zolfaghari, 2010).

Drug pricing should be designed to improve patient's access to the drug without diminishing the incentive to innovate in the manufacturing sector (Jonsson & Wilking, 2014). In all industries, the goal is to determine an optimal exchange of incentives for innovation, customer protection, and value for money (Levaggi, 2014). Besides, at the time of pricing, it must be determined whether the producer's increased funding is important or whether the price of the drug is lower so that the patient can afford it and promote community-based health (Drummond et al., 1977). The price of the medication should be set in such a way that the incentive for innovation is not lost on the manufacturer (Jonsson & Wilking, 2014). It is also recommended to introduce a risk-sharing scheme when prices are set using a value-based scheme (Levaggi, 2014). At the time of pricing, one should pay attention to the surplus value that can be generated related to production because if the price is set high, producer income and investment in future research will increase (Drummond et al., 1977).

Sunil Shrestha et al. (2020) studied price variation among different brands of anticancer medicines available in hospital pharmacies of Nepal. Akhlaghinia et al. (2018) proposed a system dynamics model for the Internet of Things (IoT) in the Pharmacy industry. They have investigated the typical production logistic execution processes and adopts system dynamics to design cost-effective IoT solutions. Darabi, N., and Hosseinichimeh (2020) conducted a systematic literature review of system dynamics applications in health and medicine published between 1960 and 2018. SD contributions to three areas of disease-related modeling, organizational modeling, and regional health modeling are studied as well. In an article entitled "a simulation model to evaluate pharmaceutical supply chain costs in hospitals: the case of a Colombian hospital," Franco (2018) develop a simulation model that allows decision-makers in hospitals and governments to identify the variables that affect the final cost of medicines and to determine the legal reimbursement allowed by national agencies. Yaghoubi and Hayati (2018) studied the system dynamics model for analyzing the bullwhip effect in the drug supply chain considering a targeted subsidy plan. Hill et al. (2018) studied estimating production costs and potential prices for the WHO Essential Medicines List. A summary of researches most related to this study is summarized and presented in Table I.

III. MOTIVATION AND RESEARCH OBJECTIVE

The literature review indicates that the production of medicine requires the attention of management using new technologies while focusing on procuring sufficient raw materials promptly. A comprehensive approach taking a look at the production cost, the volume of production, quality of medicine, producers' profit, and the end producing the price of medicine lacks in the literature. Hence, this gap demanding research to be conducted. In this regard, these authors set the objective of this study to be "the presentation of a system dynamics approach that can depict the trend of producers' profits over the periods in such a way that the volume of production and the quality of a medicine can be increased and the production cost which is the key drivers of the medication's price, can be decreased. Table II is presented for clarification purposes to show the place of this research and its contribution to the literature.

Table I. Factors Affecting Medication Pricing

Reference	***Title***	***The objective of the study***	***Associated factors***
(Amini & Zolfaghari, 2010)	analysis of factors affecting the total productivity of production factors a case study of the Iranian pharmaceutical industry	investigating the factors affecting the total productivity of manufacturing factors with emphasis on human capital, technology, and management indexes in 7 selected pharmaceutical industries in Iran between 1998-2005	government subsidies for pharmaceuticals, production financing, production investment, supply of raw materials, production costs, production volume, productivity, advertising and marketing, people's attention to the brand, medication quality, competitiveness, production capacity, human resources, technology, technology, research, and development
(Robinson & Howell, 2014)	specialty drugs: policy initiatives improving evaluation, pricing, prescribing, and using	analysis of the five main steps that a specialized medication takes from the laboratory to the use of the disease and the impact of the structures of each stage on the value of the medication	distribution costs
(Mousnad et al., 2014)	a systematic review of factors affecting drug costs	digestion of the key factors affecting the increase in pharmaceutical costs	advertising and marketing, inflation rate

Continue Table I. Factors Affecting Medication Pricing

Reference	*Title*	*The objective of the study*	*Associated factors*
(Garattini et al., 2007)	pricing and reimbursement of proprietary drugs in seven European countries: a comparative analysis	the valuation of the laws used by governments to potentially reward innovative medications	investing in research and development, producer profits
(Babar et al., 2007)	evaluating drug price, availability, affordable price and price components: implications for drug access in Malaysia	the importance of distributors and retailers profiting and monitoring people's medical costs	production costs
(Abdollahiasl et al., 2014)	a system dynamics model for national medication policy	investigation of national medicines policy in Iran using a dynamic systems approach	government subsidies for pharmaceuticals, production financing, production investment, supply of raw materials, production costs, production volume, productivity, advertising and marketing, people's attention to the brand, medication quality, competitiveness, production capacity, human resources, technology, technology, research, and development
(Ebadi & Ghavam, 2009)	targeting medication subsidies from both justice and employment perspectives	investigating the process of targeting medication subsidies in Iran during 1995-2003 and efficiency changes in the pharmaceutical industry sector	government subsidies for pharmaceuticals, production financing, production investment, production capacity, competition, medicine quality, human resources, profits, exchange rate
(Kalantari et al., 2014)	investigating the effect of subsidy targeting plan on the supply chain using systems dynamics	designing an appropriate model to investigate the impact of cash subsidy distribution on people's satisfaction with drug changes and the impact of the distribution of this type of subsidy on the total profit of the supply chain	the inflation rate, wages, human costs, energy costs, technology, technology costs, raw materials costs, producer profits, production costs, exchange rates, drug distribution, medication taking

Table II. Reported studies with MCDM methods in association with Medicine production and pricing

	MADM approaches	*MODM approaches*	*Systemic and simulation approaches*	*Statistical approaches*
Medicine Production analysis	X	X	This study	X
Medicine pricing	X	X	System dynamics (this study)	X
Integrated Production and pricing system	X	X	Systems thinking, SD (this study)	Regression, multi regression, Structural-mathematical modeling, statistical methods
Scenario analysis and performance evaluation	X	X	Scenario analysis through SD (this study)	X

IV. SYSTEM DYNAMICS

The structure of the system gives rise to a specific group of behaviors. This difference in attitude is significant because it represents the whole system's view and the components' relationships to each other. Instead of just looking at some of the factors and knowing their impact, systematic thinking is how to apply the holism approach. It is a framework that focuses on understanding the internal relationships of phenomena rather than identifying them individually, perceiving change, and not static cognition (Senge, 2016).

A systematic approach teaches us that there are two types of complexity in the world, “complexity in detail”, which encompasses a large number of variables, and the other “complexity in dynamics”, where the effects and consequences of causal relationships between the various factors of time and place considerations do not come close to each other, so precise arrangements will not lead to expected results (Senge, 2016). Balancing between increasing market share and developing product or service capacities, gaining price, quality, and competitiveness in the marketplace are all dynamic issues (Senge, 2016).

System dynamics is an analytical modeling approach rooted in cybernetics and simulation concepts.. However, the system dynamics were undoubtedly laid out in 1950 at MIT by Jay Forster in his first work on “industrial dynamics” (Brailsford, 2008). “System dynamics” models currently cover a wide range of areas related to social issues, including health, energy, environment, social services, scarcity of resources, security, and many other related areas (Ghaffarzadegan, et al, 2011).

System dynamics is used by Liu, et al. (2018) to evaluate cost-effectiveness of treatment options for diabetes patients. Ghaderi used SD to study biodiesel and bioethanol supply chain system. Zare Mehrjerdi (2013b) used SD for weight analysis and evaluating the impacts of body weight on heart problem and heart attack. In another study, Zare Mehrjerdi (2013a) employed systems thinking concept for analyzing the impacts of RFID technology on healthcare system problem. Deborah A.D. Marshal et al. (2015) used dynamic simulation modeling in health care delivery research. Eftekhari and Zare Mehrjerdi (2017) developed a SD model to investigate the losses due to medicine consumption cycles. Zare Mehrjerdi, Alemzadeh, and Hajimoradi (2020) developed a system dynamics approach for analyzing the impacts of health related factors on economic growth. Najafi, et al. (2019) developed a SD model to explore the role of lean thinking in sustainability of healthcare supply chain in Shahid Sadoughi Hospital in Yazd. A system dynamics approach to healthcare cost control was developed by Zare Mehrjerdi in 2012.

Therefore, in this study, given the ability to use system dynamics in a comprehensive and integrated manner through modeling and simulating complex systems to understand the consequences that current and future policies would have on the system is considered an appropriate opportunistic approach.

V. PROBLEM DESCRIPTION AND NECESSITY OF RESEARCH

In a pharmaceutical production system, the producer faces increasing production costs on a day-to-day basis for raw material costs, R&D expenses, equipment, technology changes, and expert manpower requirements. Often, they work with limited resources or substitute low-quality materials for various reasons. Financing return, which includes both producer and investment profits, should enable manufacturer marketing to the community based on financial resources and increasing costs. The resources and costs of medicine are influential factors that need to be integrated individually for examining the impacts of the changes occurring in subsystems.

Health is one of the three basic human needs, and medicine is the most crucial complement to the patient’s treatment cycle. The steps that the drug takes to reach the patient are medication production, medication distribution, physician prescribing, and medications use by the patient. One of the most important stages is medication production, however. In the medication production system, the financier with the manufacturer must be able to provide people with the desired quality drug and also manage the cost of production that generates the basic price of the drug so that the patients can afford it. Therefore, the manufacturer faces various issues such as the cost of drug production, the manufacturer’s funding, the volume of production, etc., each of which directly or indirectly affects other sectors. For better decision-making in the drug production system, factors affecting each of these subsystems need to be identified, and their relationships within the subsystems and the relationship of each subsystem to the other subsystems investigated to make better decisions. According to our previous discussions, the use of dynamic systems approach can be effective.

VI. SOLUTION STEPS IMPLEMENTATION

This section follows all the steps listed below for solving medicine production using the system dynamics approach. The steps are: (1) Determining key variables, (2) Determining the system boundary by specifying endogenous and exogenous variables, (3) Providing a dynamic hypothesis, (4) Drawing a causal diagram of the problem, (5) Drawing flow charts, (6) Mathematical Modeling, (7) Simulation and validation, (8) Policymaking and scenario presentation. Figure 1 schematically shows how this research is done from literature review to scenario development and analysis.

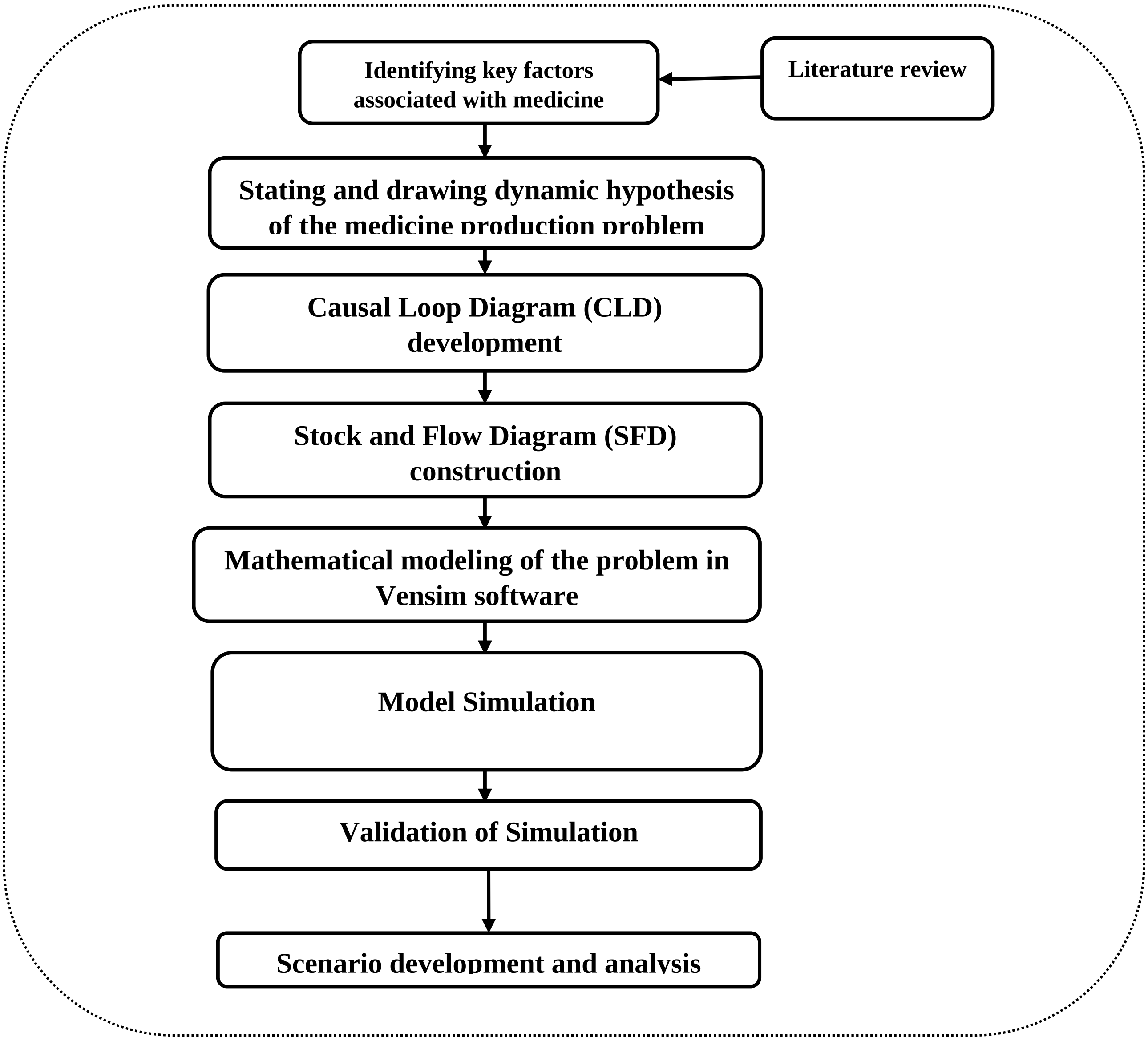

Fig. 1. Steps to follow medicine production and pricing study using system dynamics

Steps 1 (Determining key variables)

The key variables taken into consideration for causal diagram model development were gathered from two main sources. First, using literature review, authors were able to identify variables used or suggested by other researchers in their work. Second, to have all necessary variables for our problem, additional variables were added to the listed and consulted with the experts on the subject matter for their appropriateness.

Step 2 (Boundary of the system)

The model boundary is summarized by listing endogenous, exogenous, and variables that are not considered in the model but may be relevant to others. For the problem under discussion, the model boundary is determined by the variables given in Table III.

Table III: key variables and model boundaries

Exogenous variables	*endogenous variables*	*Others omitted variables*
Investment	Customer satisfaction	Raw material supplier
Financial sources	Production vacancy	Medication waste
Human Wages	Amount of raw material needed per capsule	Insurance charges
Human source	Number of The multiplicity of human resources	
Expenses human	Inflation rate	
Prices of raw materials	Rate of currency	
Supply of raw materials	Depreciation	
Supply of raw materials Expenses	Energy expenses	
Production capacity	Other expenses	
Production expenses	Producer Profit Margin Percentage	
Producer profit	Pharmacy Profit Margin Percentage	
Medicine Distribution	Distributor Profit Margin Percentage	
Distribution expenses		
Medicine price		
R & D		
Medicine quality		
New Equipment and technology		
Efficiency		

Step 3 (Dynamic Hypothesis)

The dynamic hypothesis is a depiction of a cause and effect diagram showing important feedback loops and main variables and/or subsystems of the problem. Based upon previous studies, it is expected that concerning production costs, financial resources, producer profits, and production volumes that are related to drugs; one can consider relevant subsystems in the field of production so that drug prices can be assessed. The producer should profit enough to manage to supply the community with a sufficient amount of drugs they need. Figure 1 is a representation of the dynamic hypothesis of the problem.

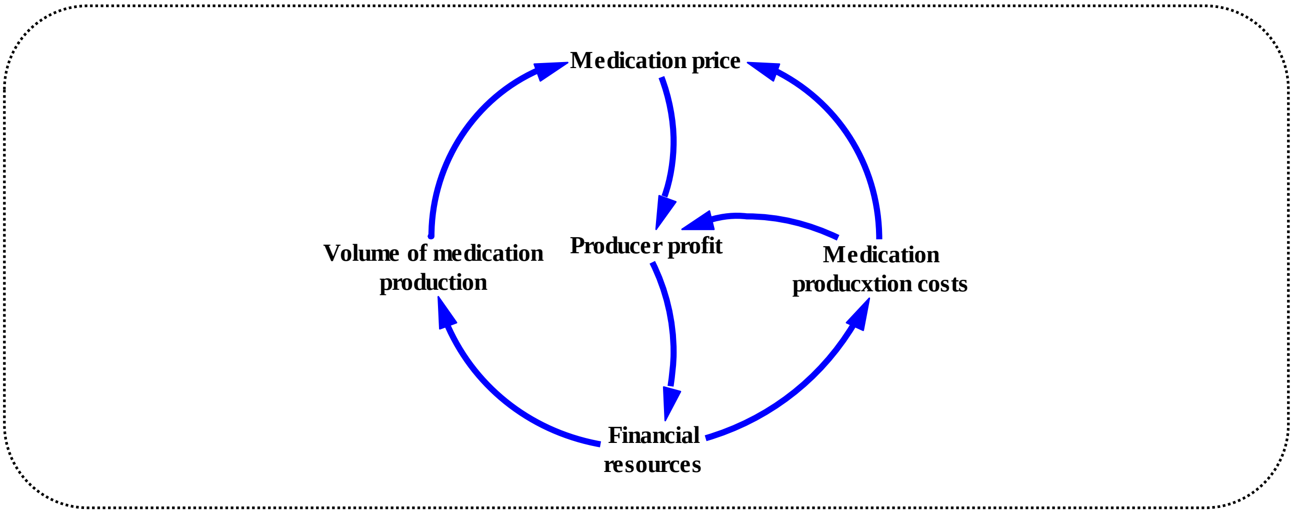

Fig. 2. Dynamic hypothesis of the problem

Step 4 (Cause and effect diagram)

Systematic thinking means every action may be considered with both cause and effect phenomena. There is no one-sided action (Senge, 2016). Causal links between variables are assigned a positive (+) or negative (-) sign indicating polarity. A positive sign means that cause and effect changes have the same directions, and a negative sign means the opposite direction of cause and effect changes. The feedback process is divided into two distinct types: reinforcing and balancing. The variables and their feedback relationships are presented in the form of a causal graph in Figure 2. Some of these loops are described in more detail below.

A. Feedback loops of raw material supply

Feedback loops related to the supply of raw materials examine the impact of raw material supply costs that makes a large part of production costs. With increasing factory finances, raw material supply based upon production capacity and raw material prices increases, leading to increased raw material supply costs and increased production costs. Producer profits increase as profits are considered as a percentage of production costs. The increase in producer profits will also give rise to increased factory finances. Increasing the financial resources of the producer, the producer will provide more quality raw materials. The higher the quality of the raw materials, the higher the price of the raw materials, resulting in increased production costs, producer profits, and financial resources. Figure 3 presents the feedback cycles associated with the raw materials.

B. Feedback loops relating to customer satisfaction

Due to increasing producer funding, R&D will increase. So, with a higher R&D, more quality medicine will be produced and ultimately customer satisfaction, investment, and funding will increase. As the financial resources increase, the manufacturer will make more quality raw materials, thereby producing more quality medicine that will increase customer satisfaction. Increased customer satisfaction will increase investment and increase investment in financial resources. Figure 4 shows the feedback cycle of customer satisfaction.

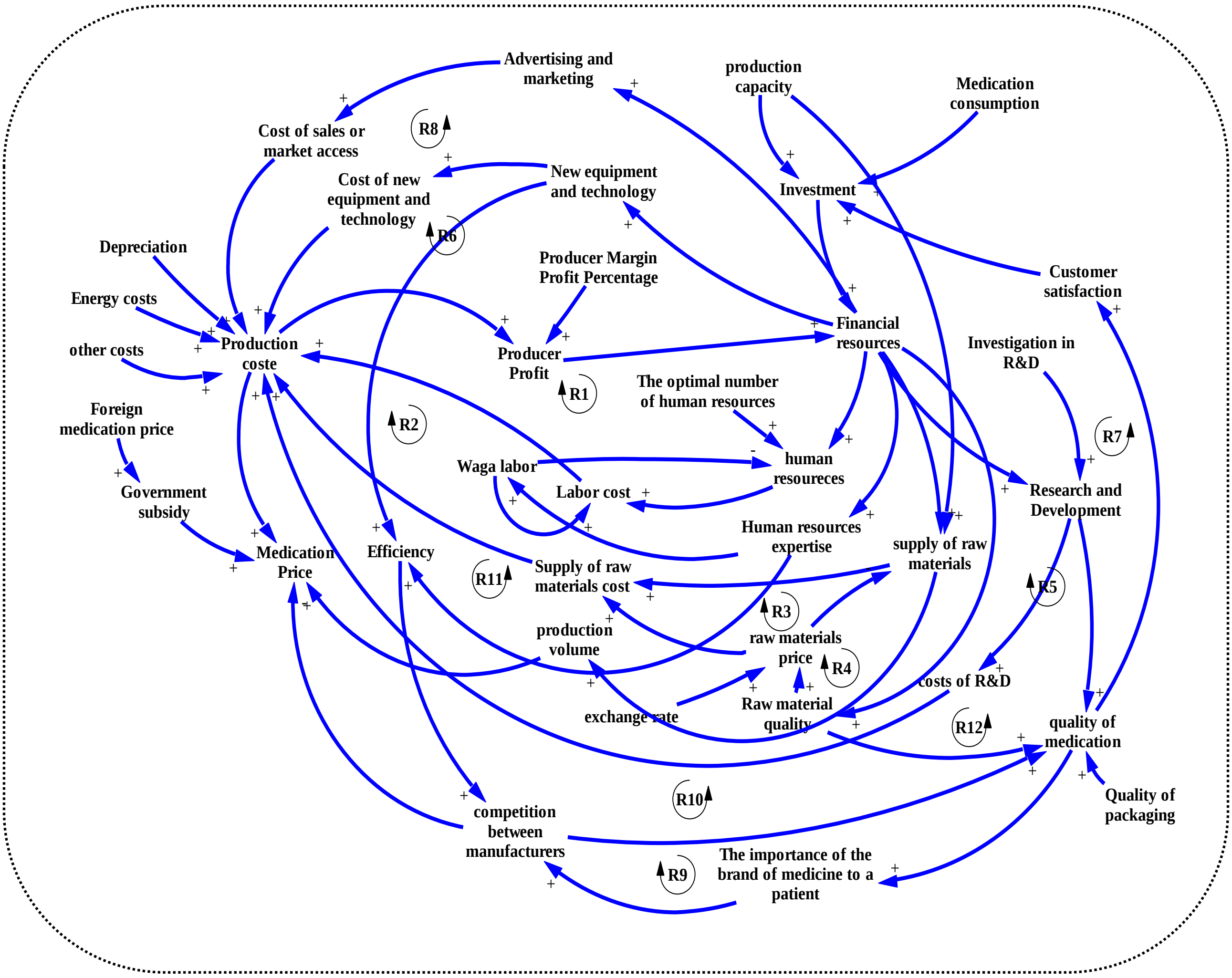

Fig. 3. Causal loop diagram for medicine production and pricing

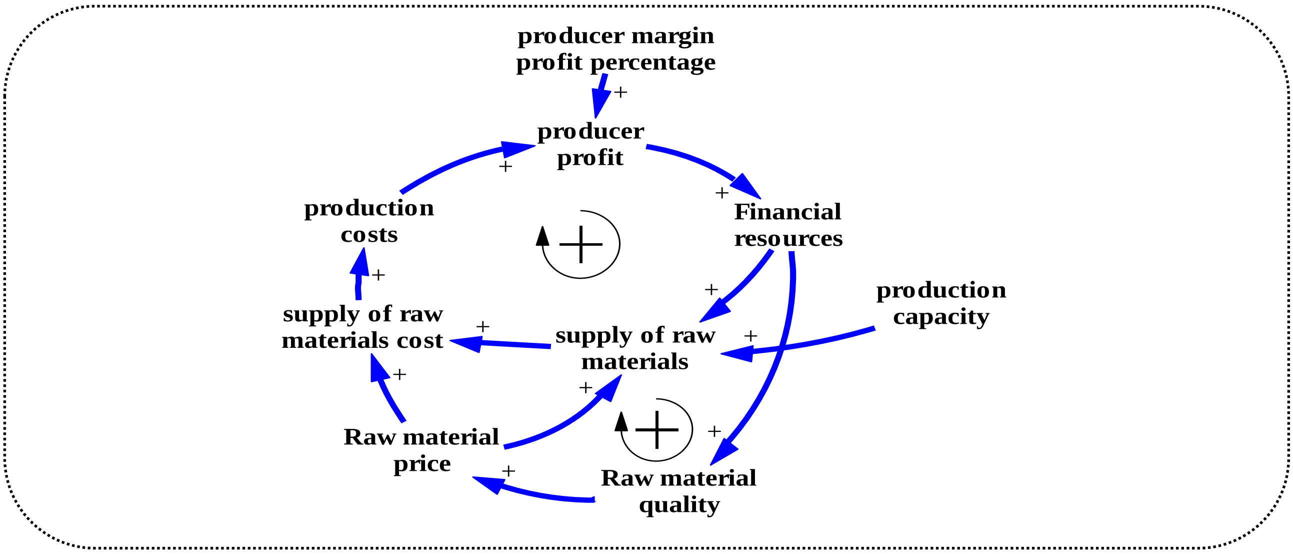

Fig. 4. Feedback loops for raw materials

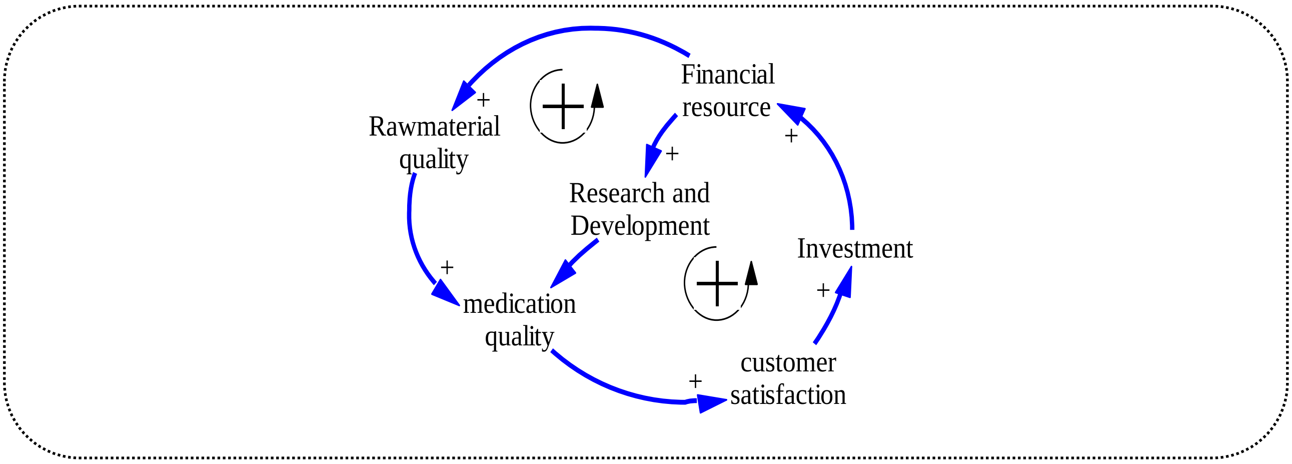

Fig. 5. feedback loop for customer satisfaction

C. Feedback loops relating to new equipment and technology

The equipment and technology feedback loop indicates that as new funding increases, new plant equipment and technology will increase. Increasing new equipment and technology increases technology costs and increases production costs, profits, and financial resources. Figure 5 shows the feedback loop of new equipment and technology.

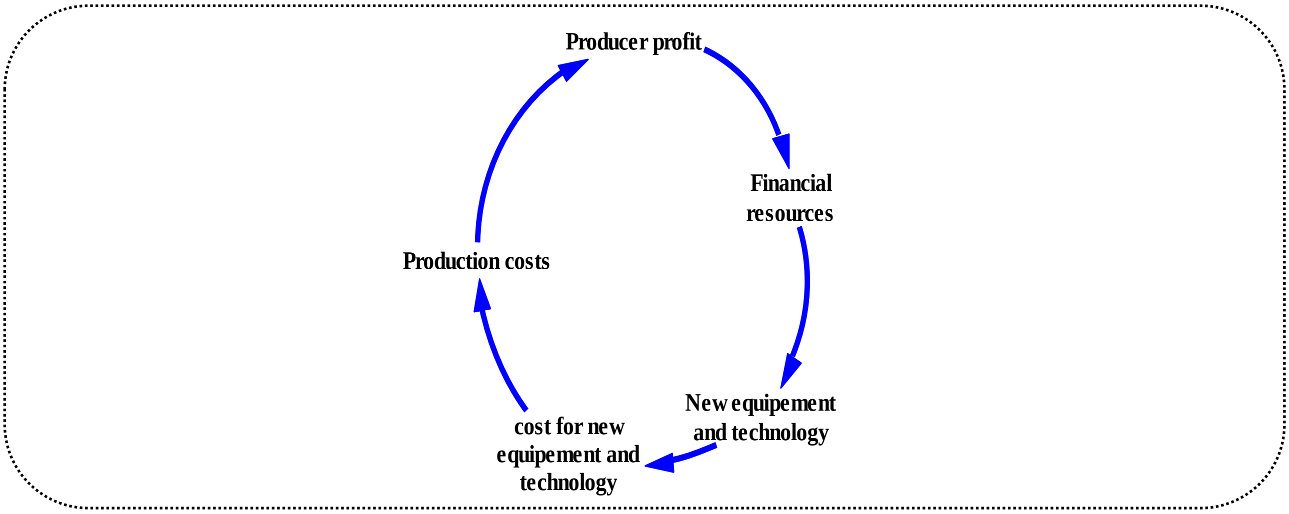

Fig. 6. A feedback loop of new equipment and technology

It should be noted that R&D and market access factors are more related to the brand (generic) and brand-generic drugs that cannot be considered for generic drugs. Figure 6 shows the generic medication for advertising and marketing.

Step 5 (Stock and flow diagram)

Stock and flow diagram is the complete chart used in modeling part of problem using system dynamics approach. This chart allows us to have all the needed details for writing the equations necessary in the simulation. To draw a flowchart, firstly, it needs to specify the type of variables. Variables in dynamic system models are categorized into three levels: level variable (state), rate variable (flow), and auxiliary variable. Level variables are variables that accumulate in them occur and are measurable at each moment. Input or output variables for level variables are rate variables that can be measured over a specified time. Auxiliary variables define the details of a system for clarification purposes.

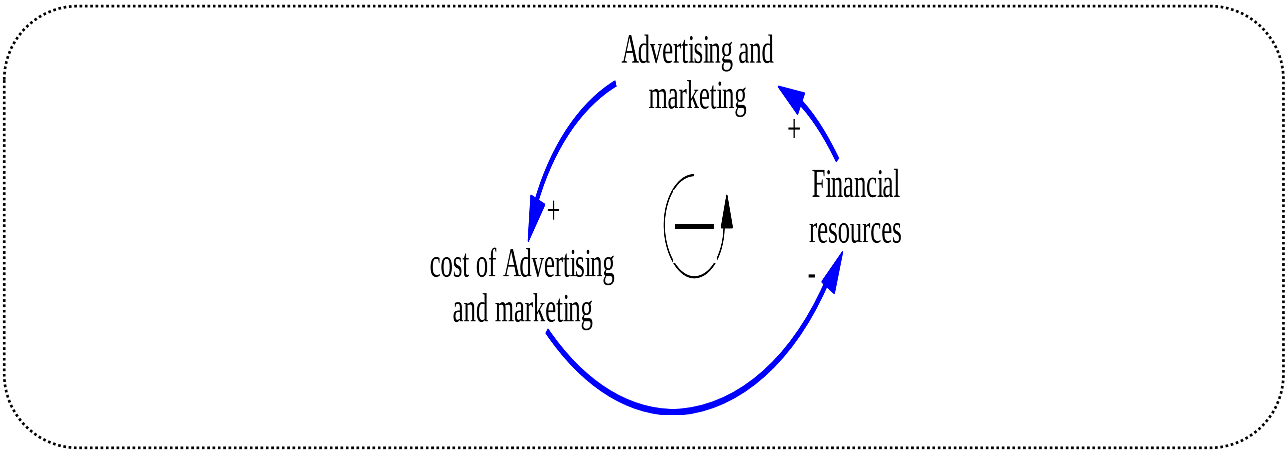

Fig. 7. Generic medicines for advertising and marketing chain

Steps 6, 7, and 8 are discussed in more detail as the solution process for the case study continues.

VII. CASE STUDY (AMOXICILLIN CAPSULE) AND DATA SELECTION

In the present study, to perform simulation, it needs determining a kind of medicine and related data of its production. So, for this purpose, amoxicillin capsule has been studied, and relating production data have been obtained by Kosar Pharmaceutical Company (Bank Brokerage Company, 2014). Amoxicillin is a generic medicine from an antibiotic therapy class that was discovered in 1972 by scientists in the Becham Research Laboratories and presented to the market as an Amoxil brand (eMedExpert, 2008). Amoxicillin capsule is the second most widely used medicine in Iran (ISNA, 2013).

According to the present statistics, per capita, medicine consumption in Iran is at a high level due to the prevailing culture and relative cheapness of medicine, which is four times of global average. Unfortunately, antibiotics are one of the most commonly used inappropriate medicine that, in addition to creating microbial resistance at the community level, it causes to impose high and futile costs on a patient, the medical system, and the treatment of countries.

Today, one of the most important troubles in the medical community is the process of prescribing and overdosing on antibiotics, and also, it has a direct impact on community health, which is also economically feasible (Hossein Zadeh et al., 2016). Unreasonable administration of antibiotics, especially their overdose, increases bacterial strains in nosocomial infections and causes dangerous but avoidable complications that result in irreparable financial and clinical costs to the health system (Hajebi et al., 2005).

On average, research and development on each new medicine (and antibiotics) costs is about $ 5 billion and, according to statistics and current condition it is about 80 percent of the newly manufactured medicine do not present to the pharmacy market. The cost of medicine for entering the pharmaceutical market is much higher and heavier. Therefore, just like any other commercial product, pharmaceutical companies prefer to market a product that has a very high production range. In other words, it is the preference of pharmaceutical companies to spend the multibillion-dollar expense on which medicine can manufacture and market for a long time, not as quickly as the antibiotics after being manufactured. Antibiotic resistance is outdated and inappropriate (secret project, 2015).

Because the type of medicine production in Iran is generic, and because of the types of medicines and the conditions of the country, research and development, advertising and marketing, and competition have been removed from the flow chart of this medicine. In addition to that, medicine distribution is considered to be a part of the production system. Table IV lists the types of variables used in this modeling.

Table IV. the lists of variable types

Level Variable	***Rate Variable***	***Quantitative Variable***
Production costs	Production costs rate	Others expenses
Medicine price	Medicine price rate	

Based upon the cause-and-effect chart and type of medicine chosen for the case study, as well as the Iran conditions, the stock and flow diagram is created and presented in Figure 7.

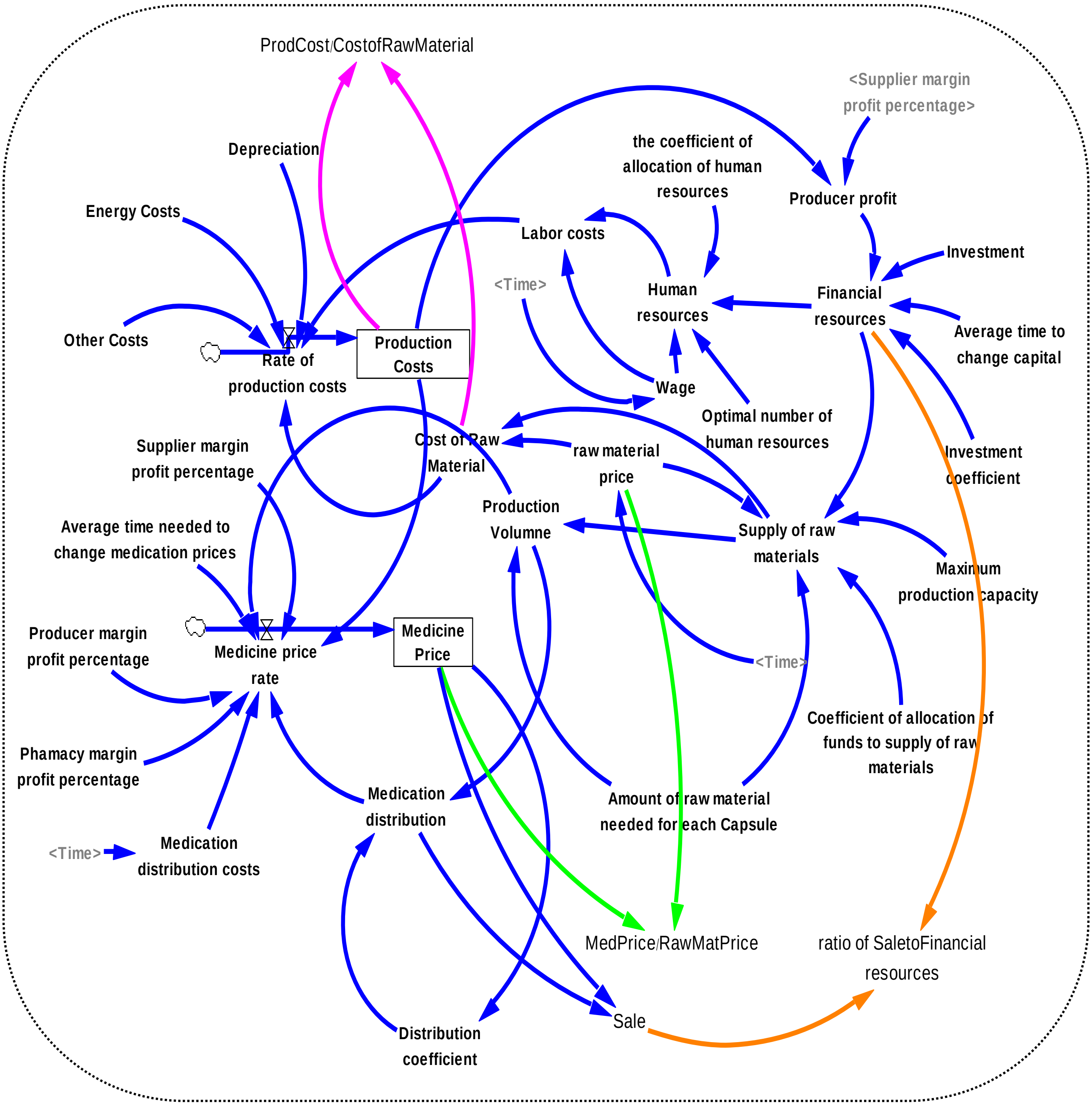

Fig. 8. Stock and flow diagram for medicine production and pricing

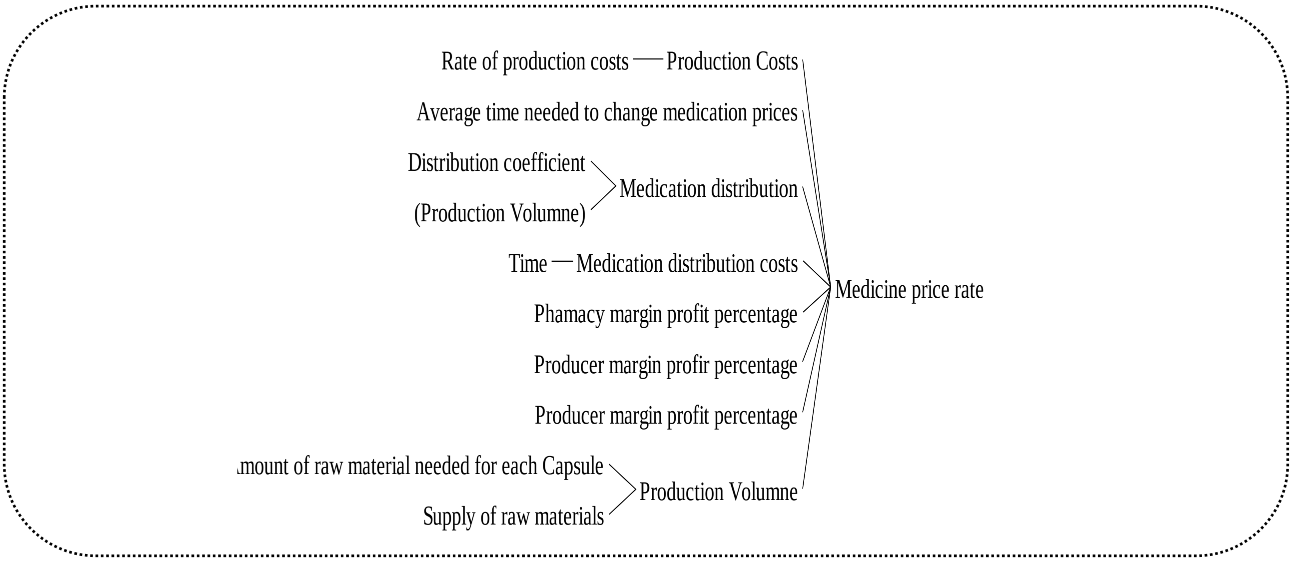

Fig. 9. factors impacts on the rate of drug price

VIII. SIMULATION, VERIFICATION, AND VALIDATION

A. Verification

There are some ways to verify the model produced in one computer simulation program, in general. Regarding system dynamics simulation, to make sure that the formula used in the Vensim is correct, the authors have checked the codes the used parameters in the program. This was double-checked by each author. To make sure the parameters and constants used in the formula are correct, values were obtained from related articles and appropriate websites, as discussed before.

B. Equations and Parameters

After drawing the flow chart and identifying the type of variables, the equations were written based upon the type of variables and the relationships among variables. After ensuring the accuracy of equations and parameters, the simulation was run with a time horizon of 10 years and a time step of one. As described in Section 1-5-5, to simulate the proposed model for the production of amoxicillin capsules, production data of Kosar Pharmaceutical Company were used. It was assumed that the price of raw materials would increase by 5% each year due to the effect of the exchange rate. In addition to that, it is assumed that the wage of manpower will increase by 6% each year due to the effect of inflation. Producer margin profit, distributor, and pharmacy are considered to be 0.2, 0.11, and 0.21, respectively. It should be noted that in this model, government subsidies are not considered. The ending cost of medicine production and marginal benefit is used to determine the cost of the finished good. The effect of medicine consumption and great demands on prices is discarded as well.

C. Validation

Validation of the models developed by system dynamics is a process of assuring utility and usefulness of the model as a policy tool. Many authors have discussed the validation of system dynamics models. Greenberger et al. (1976) claimed that “none of the models has been fully validated and it won’t ...”. However, the first step in determining the validity of a model is its suitability for the intended purpose of the study. Generally, various tests have been presented by subject literature for validation purposes. In this research, the authors use five major tests, namely: (1) behavior reproduction test, (2) structural confirmation test, (3) dimensional adaptation test, (4) boundary adequacy test, and (5) test of limit conditions.

D. Structure verification test

This test checks the suitability of the model concerning its goals and the problem that was addressed. This means that "whether the model structure is consistent with the existing knowledge of actual system's structure, and are the most relevant structures modeled?" (Teymouri, et al., 2012). Based upon the investigations made in the literature of the subject matter and necessary consultation with the field experts on model building using our presented mental model, the model structure was confirmed.

E. Dimensional compatibility test

This test is part of a fitness series of tests that Sterman and Sushil are referring to. This test determines whether the dimensions of the variables in all equations on both sides of the equation, are in equilibrium. This test was performed according to Vensim's software, and it was found that there was no discrepancy between the dimensions of variables in any of the mathematical equations used.

F. Behavior reproduction test

The average price of amoxicillin 250 mg and 500 mg from 2011 to 2016 is shown in Table V according to the Daru Bank website (www.daroobank.com).

Table V. Average price changes between 2011 and 2016

Year	*Medicine Average Price*
2011	440
2012	550
2013	700
2014	1550
2015	2100
2016	2100

According to the data of Table V, the chart of price changes was drawn using linear regression in Excel software. This figure shows a diagram that is a trend for the price of amoxicillin under investigation. The author will use figure 8 to compare this actual industry price with the simulation price generated by each scenario case later.

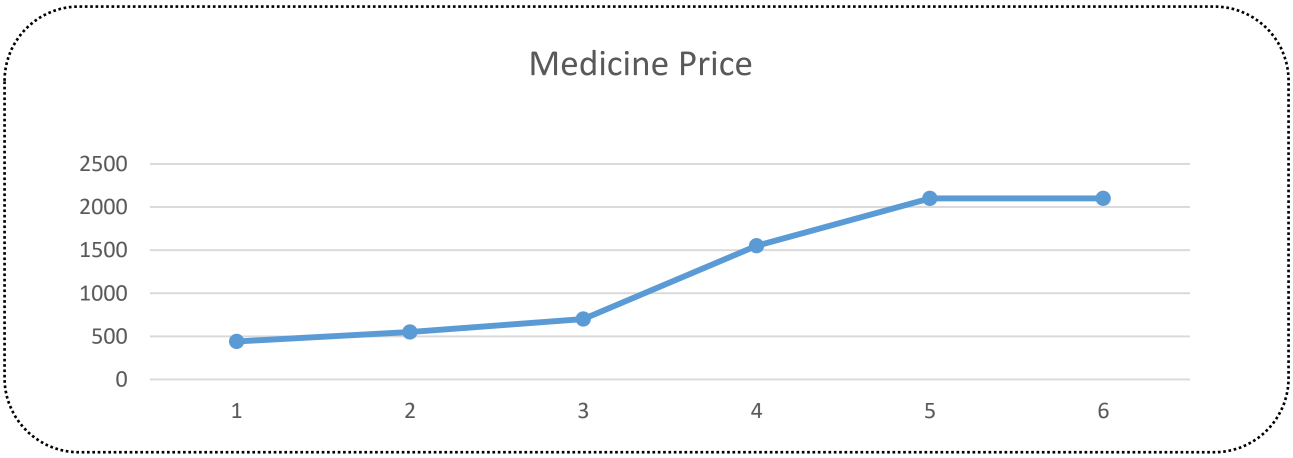

Fig. 10. Medicine price change using simple graphic

G. Border sufficiency test

The purpose of this test is to determine the level of the holism of the model. Is the model's level appropriate and encompasses all relevant structures, including the variables and effects of feedback needed to address the problem? Does this structure, with the intended boundary, fit the purpose of the study? (Teymouri et al. 2012). According to the purpose pursued in this study, endogenous variables have been taken into account, and enough exogenous variables have been applied, so this test is valid. For example, if there are conditions to increase the supply of raw materials, the production volume will increase to a maximum, as much as the production capacity allows and will never exceed that. Detailed information can be obtained from Figure 9.

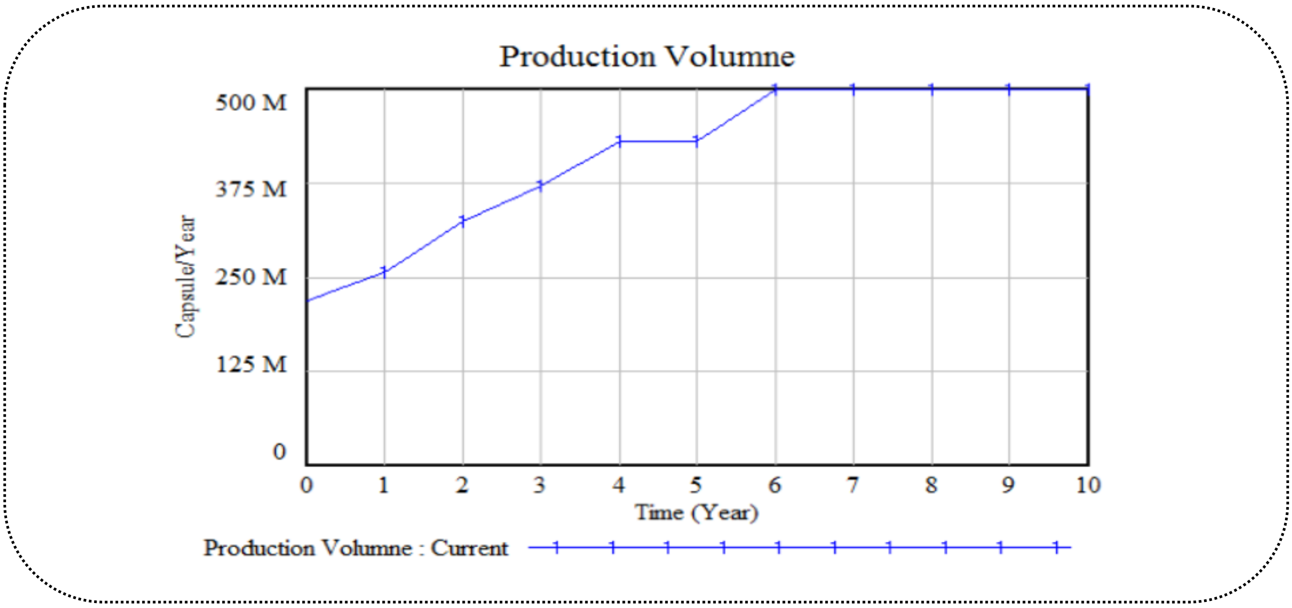

Fig. 11. An example of border adequacy test on a production volume factor

H. Scenarios

Following is the list of scenarios to be considered here.

Scenario objectives

1. Increasing producer profits and subsequently increasing production financial resource
2. Increase production volume
3. Prevent the sudden rise in medicine prices
4. Increasing the quality of the medicine

XV. SUGGESTED SCENARIOS

A. Base scenario

In the primary case, marginal profit of 0.2 and the price of raw materials is about 1000 Rials per gram. It is also assumed that producer uses raw materials with the lowest price (lowest quality). (Run 1)

B. Scenario 1

The marginal profit of the producer increases from 0.2 to 0.27, and the price of raw materials is 1000 Rials per gram. It is assumed that the government will increase the marginal profit of production from 0.2 to 0.27 due to the producers' dissatisfaction with the number of profits and insufficient funds. (Run 2)

In Figures 10 to 12, the base scenario results (Run 1) with the first scenario (Run 2) will be compared.

As Figure 10 shows, the producer profit in scenario 1 is higher than the producer profit in the baseline condition during all 10 durations. In early durations, the difference between the two graphs is low, and as it approaches the end periods, the gap widens, and the producer profits grow steeper in the first scenario.

Fig. 12. producer earning behavior in execution 1 and 2

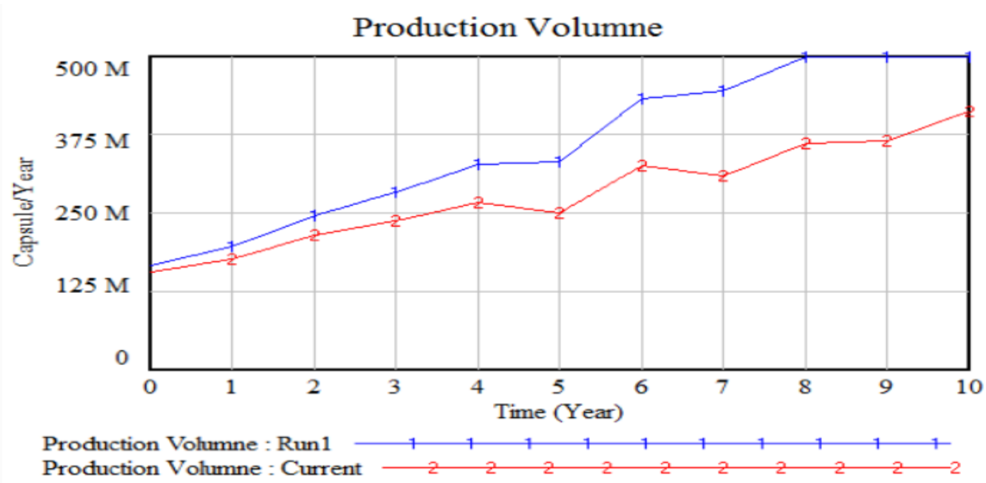

Fig. 13. production volume behavior at 1 and 2 execution

As Figure 11 shows, the production volume in the first scenario is higher than the base scenario over the whole period. The difference in production volume is low in the early years of study and increases as it reaches the end of the study period. The charts show volatility in production volumes, but the trend is upward.

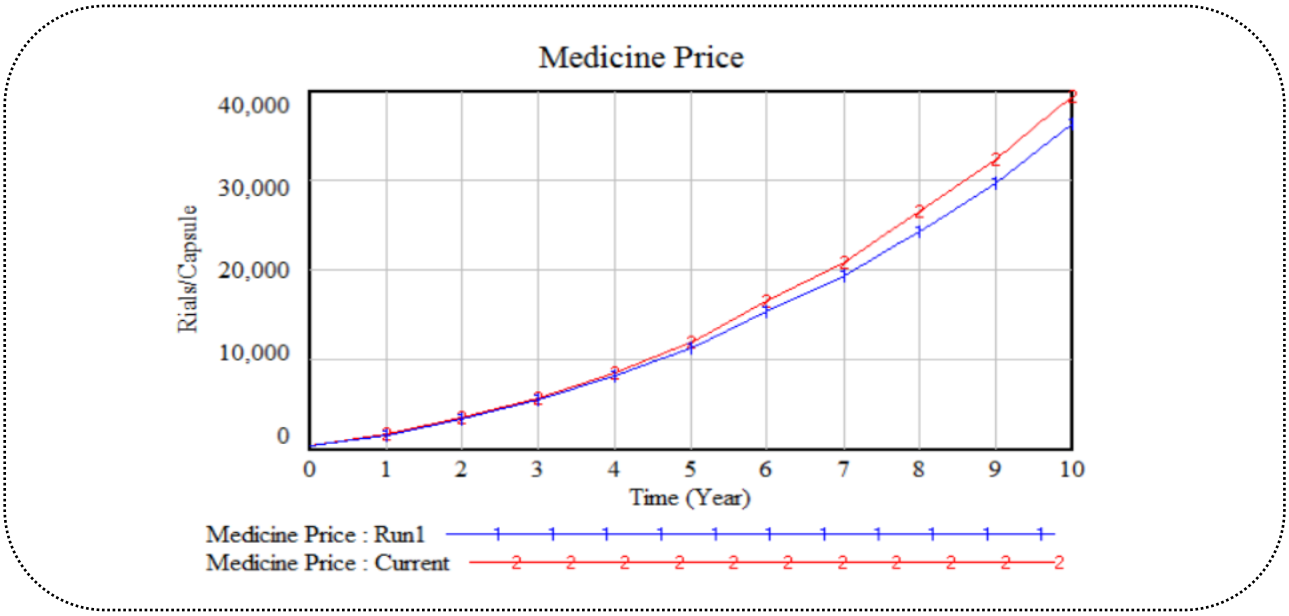

Fig. 14. Medicine price behavior at 1 and 2 executions

According to Figure 12, prices in the base scenario and first scenario are almost equal up to the fifth period. After the fifth period, scenario 1 shows lower prices as compared with the base scenario. Differences between these amounts get more evident as it reaches the end period.

C. Scenario 2

In this case, it is assumed that the profit margin is 0.27 and that the producer will procure raw material (grade 1) with a price of 1500 Rials per gram (Run 3).

In Figures 13-15, the results of this scenario are compared with the base scenario.

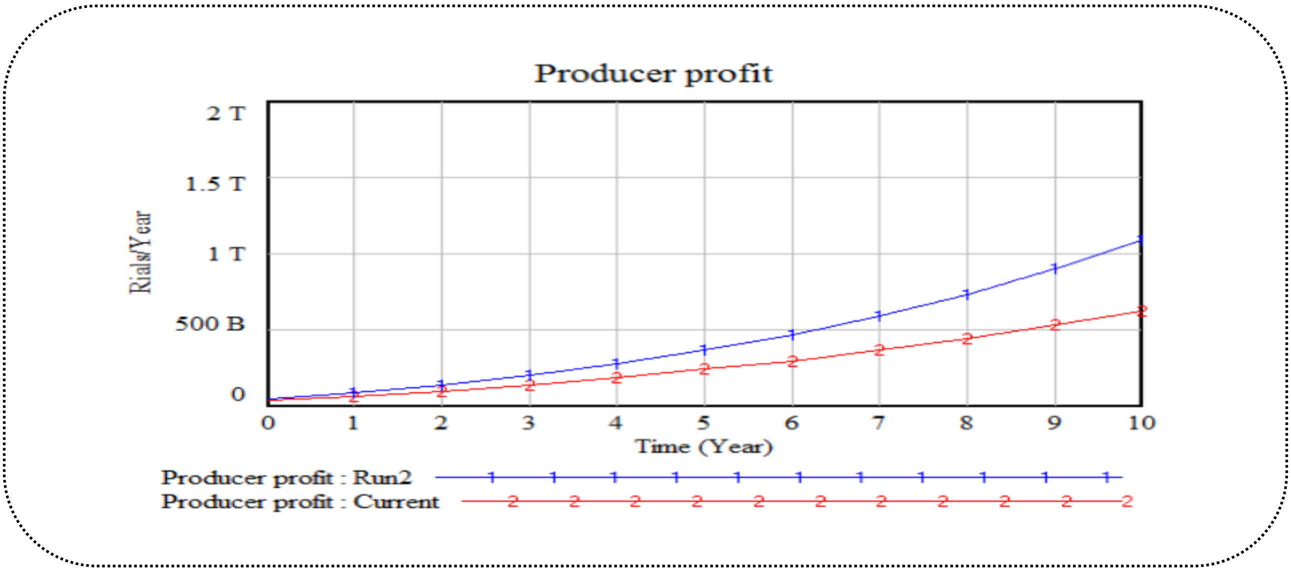

Fig. 15. producer profit behavior in executions 1 and 2

According to Figure 13, the producer's profit for the second scenario is higher than the base scenario. In the early years of this timeframe, the difference in the level of profit decreases, and the difference increases when it reaches to end periods.

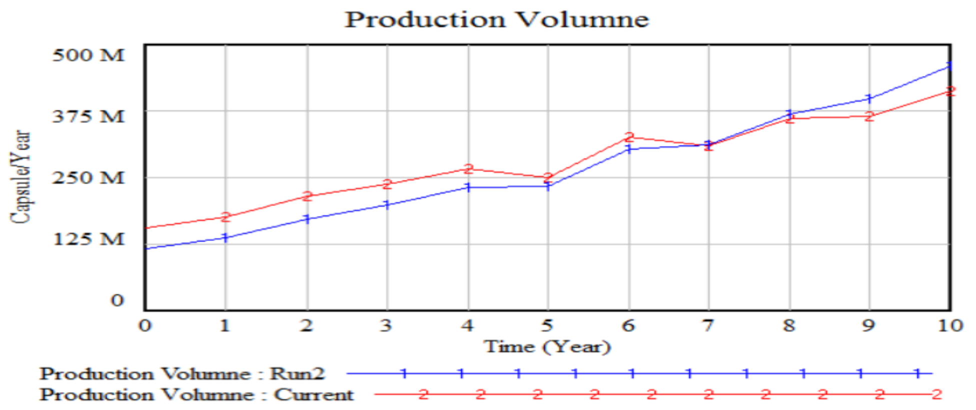

Fig. 16. production volume behaviors in executions 1 and 3

According to Figure 14, the production volume for the base scenario is higher the scenario 2 up to periods 7 and then gets lower for the remaining periods. Also, according to this figure, there are fluctuations in the volume of production. The volume of production has an upward trend over the entire study period.

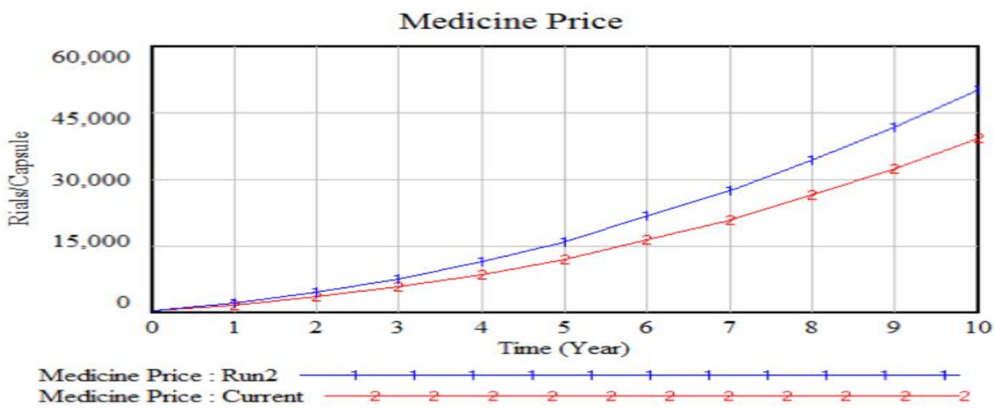

Fig. 17. Medicine price behavior in 1 and 3 executions

As shown in Figure 15, the medicine price is also higher in the second scenario than in the base scenario, and prices are approximately equal in the first two years only.

D. Scenario 3

The producer's profit margin will increase from 0.2 at the base to 0.27 and raw material prices rise from 1000 at the base to 1200 at per gram (Run 4). In Figures 16 to 18, the results of this scenario are compared with the base scenario.

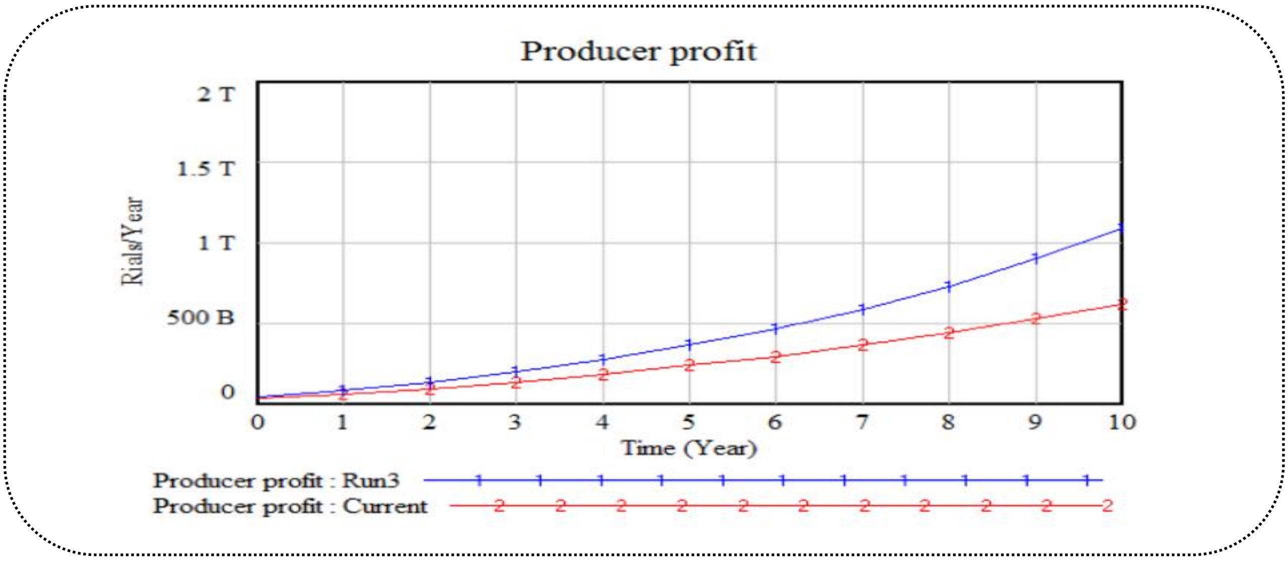

Fig. 18. Profit of producer behavior at 1 and 4 executions

As shown in Figure 16, in the third scenario, the profit is greater than the base scenario over the whole period.

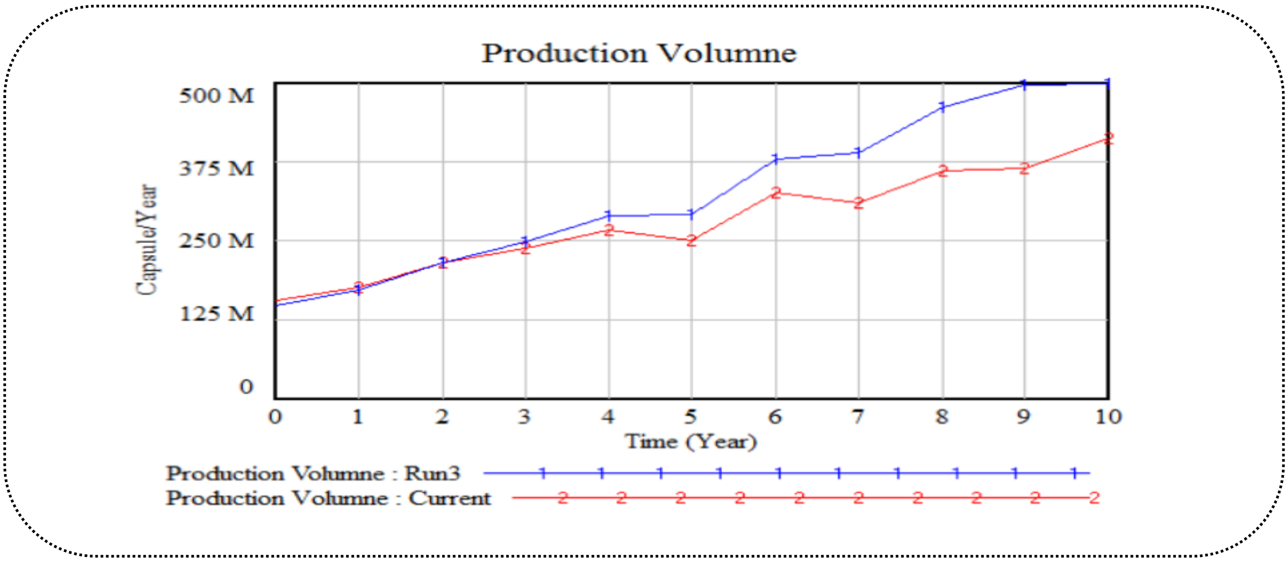

Fig. 19. Production volume behaviors at executions 1 and 4

According to Figure 17, production in the third scenario is slightly lower than the base scenario right before the second period, and after that the volume in the third scenario gets higher than the base scenario and increases yearly. Finally, in the ninth period, it reaches its maximum capacity, which is the maximum of its production capacity.

E. Scenario results and comparison

The simulation results for the base scenario and scenarios 1, 2, and 3 are now presented in a graph for comparison purposes. According to Figure 19, the producer profit in all three modes of run 2, run 3, and run 4 is the same and is upper than run 1.

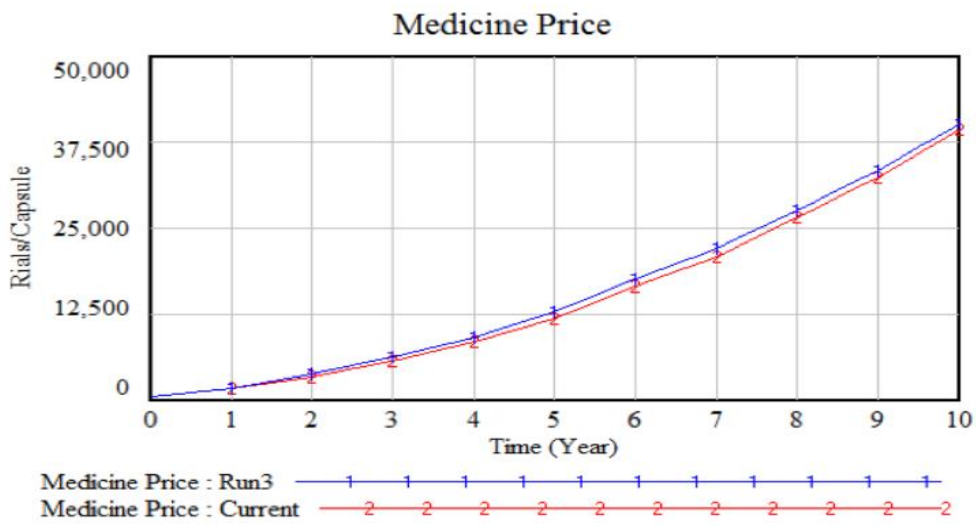

Fig. 20. Medicine price behaviors for executions 1 and 4

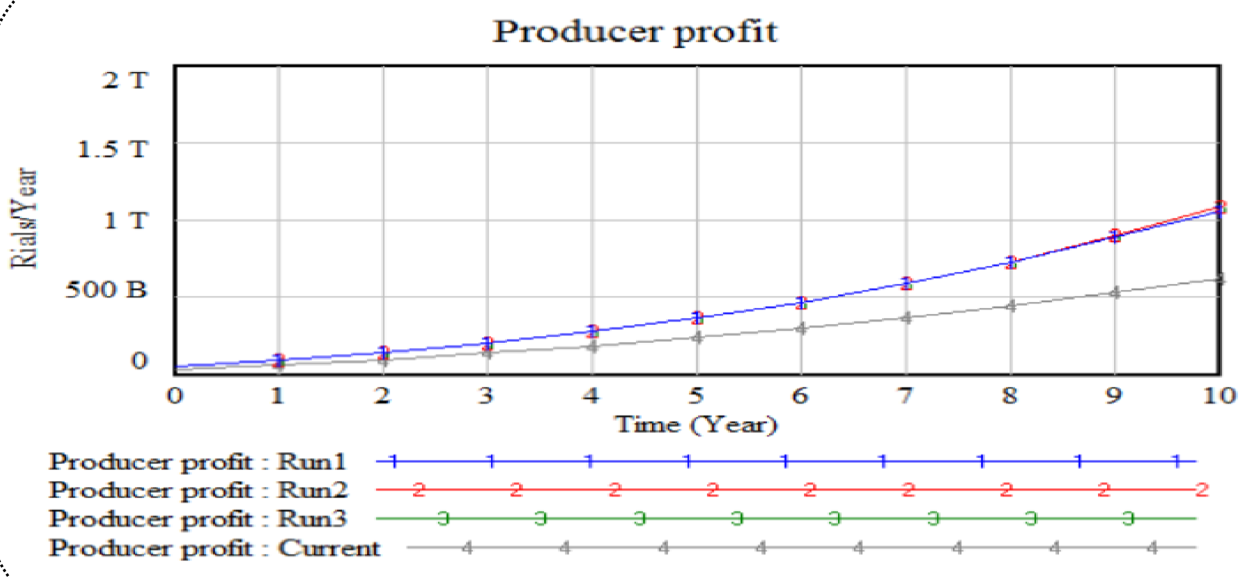

Fig. 21. producer profit in different scenarios

As it is shown in Figure 20, scenarios 1 and 3 do deal with higher production volume as compared with other scenarios. In these cases, the production volume reaches the maximum production volume possible. Finally, simulation results show that the medicine price for scenario 2 is higher than other scenarios, while the other three scenarios show closer prices for medicine.

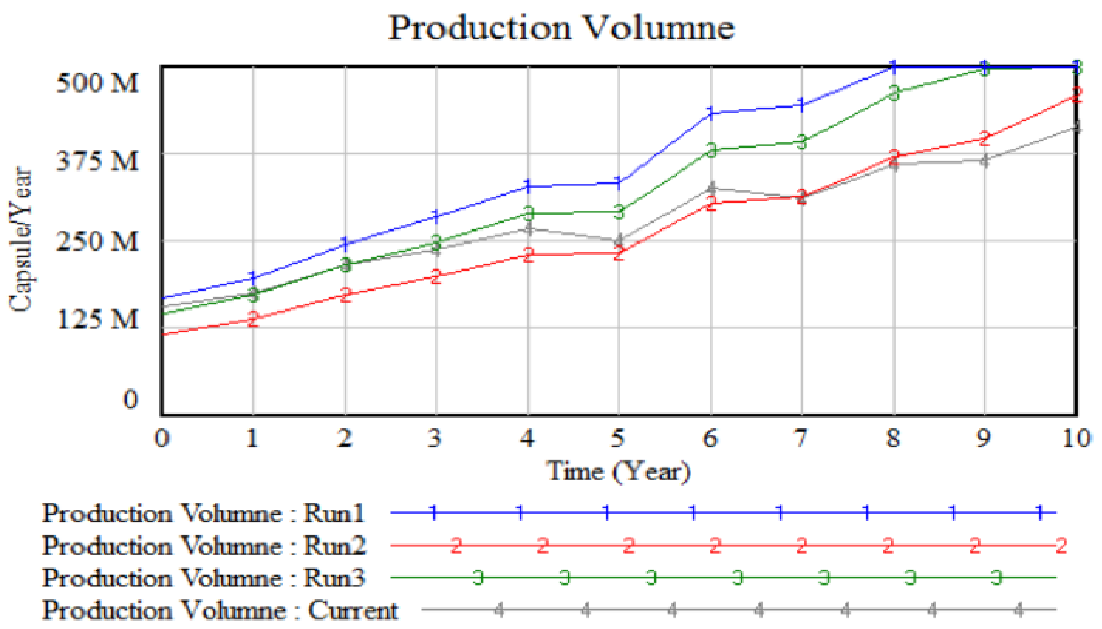

Fig. 22. production volume in different scenarios

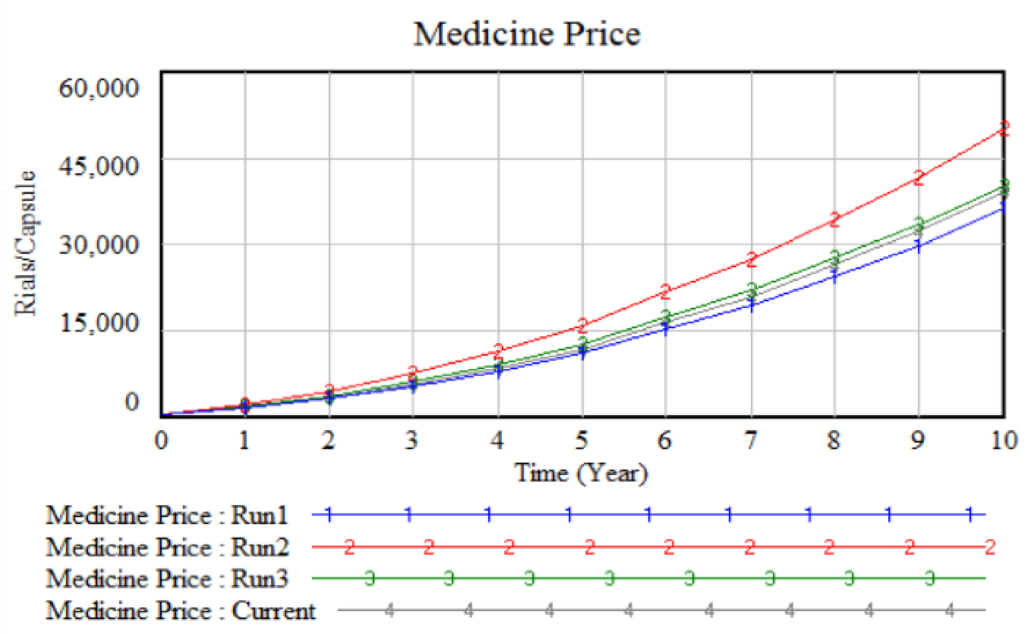

Fig. 23. Medicine price in different scenarios

XVI. SENSITIVITY ANALYSIS

Sensitivity analysis is a suitable approach for understanding how much a model is sensitive to the parameters' values and the small changes that might be made to the modeling structure of the problem. When a model is very sensitive to the changes of the key parameters, then it is hard to trust the results of that. Three types of sensitivity analysis are possible to do, as are described by Sushil (1993). These are (1) numerical-based sensitivity, (2) behavioral-based sensitivity, and (3) policy-based sensitivity. In this study, the authors concentrated on numerical-based sensitivity analysis of three main parameters which are very critical to the final medicine price. These parameters, as they are shown in the stock and flow diagram, are pharmacy margin profit percentage (PH), producer margin profit percentage (PR), and supplier margin profit percentage (SP).

Table VI. Numerical sensitivity analysis on PH, PR, and SP parameters

	Pharmacy margin Profit (PH)	*Producer margin profit (PR)*	*Supplier margin profit (SP)*	*Final Medicine Price*	*Final Rate of change*
*1	0.21	0.11	0.27	40601	7753
2	0.19	0.11	0.27	40105	7657
3	0.23	0.11	0.27	41098	7850
4	0.21	0.09	0.27	40105	7656
5	0.21	0.13	0.27	41097	7850
6	0.21	0.11	0.25	41815	7282
7	0.21	0.11	0.29	42874	8341
8	0.19	0.09	0.27	39609 **	7559
9	0.20	0.10	025	41298	7190
10	0.20	0.10	0.27	41765	7657

* Parameters used in the base simulation generating medicine price of 40601

** the lowest medicine price

Table 5 shows the results of sensitivity analysis made on parameters PH, PR, and SP. Table's first row shows the values of these parameters, as they were used in the Vensim computer simulation, having results presented in the based model. Rows 2 through 10 show the results of sensitivity analysis made on these three key parameters. Each parameter is changed by -2 percent to +2 percent. Medicine's lowest price in the 10th duration occurs once PH and PR values are reduced by 2 percent while the supplier gets the same profit margin rate of the base model. Going with this decision, we would make two of our business partners unhappy. So, it is an unwise decision to make. Situation 2 and 4 deal with one change in the value of one parameter and reduces significant changes to the base price as compared to the price value in the table's first row. Perhaps, the best decision is to keep our producers happy and let the pharmacy take the cut on the profit margin and hence choose the results of the second row with a medicine price of 40105. Therefore, the final values of profit margin for pharmacies, producers, and suppliers are 19, 11, and 27 percent, respectively.

XVII. CONCLUSION AND FUTURE STUDIES

The approach used in this research is based upon systems thinking, for developing the cause and effect diagram and system dynamics, to simulate the model and analyze the results generated. The simulation was carried out using VENSIM software on the Amoxicillin capsule as a case study. Based on the present study results, if the government increases the marginal profit percentage of the producer, and the producer also supplies high-quality raw materials. The companies` profits, production volume, and medicine quality will increase to an acceptable level. For this reason alone, this article makes a significant contribution to the Pharmaceutical fields and hence to the patients and health industry, in general. Simulation results of four scenarios are presented through figures 10 to 21. Knowing that the producers' profits in scenarios 2, 3, and 4 are the same, the decision can be made based upon the production volume and medicine price, however. In scenarios 2 and 4, the volume of production after a few years reaches its maximum value, and the price of medicine gets lower with the lower slope. Between scenarios 2 and 4, the better scenario is 4. This is because the price of medicine is slightly higher than scenario 2, which is a good factor for controlling the consumption of medicine. As the cause and effect diagram shows, once the quality of raw materials is high, the medicine would have better quality as well. And, this condition is true in scenario 2. Medicine production is a complex system incorporating various sectors of industry and society together. A complex system is defined as a system that is adaptive to changes in the local environment, and it is composed of other complex systems behaving in a nonlinear fashion and exhibits emergent behavior (Marshall et al., 2015). One of the limitations of this model is not seeing the role of final production inventory and raw material inventory for the medicine production system. This means that the proposed system is expandable for future research by interested researchers, however. In this problem, not only the producer should consider production requirements into consideration, the quality of product, the safety of medicine, the impacts of medication on patients, sufficiency of raw materials, on-time availability of raw materials, importing rules limitations, and so on must be taken into consideration. So, in the present study, factors such as medication safety, medication side effects, and raw material supply may be taken into consideration for model expansion and future studies. Also, the proposed model can be expanded by considering multi-sourcing for raw materials and systems resiliency for dealing with risk factors due to various distributions that may occur for the production-distribution-consumption system.

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