ISSN : 2455-9679
SJIF Impact Factor : 6.008

IJRTSM
INTERNATIONAL JOURNAL OF RECENT TECHNOLOGY SCIENCE & MANAGEMENT

"DEMAND FORECASTING FOR PHARMACEUTICAL INDUSTRIES EMPLOYING ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING APPROACHES: A SURVEY"

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ABSTRACT

Off late, the demand for pharmaceutical products and drugs has ramped up significantly due to the ongoing COVID-19 scenario. Several instances have been reported where large scarcity of drugs have led to fatalities in patients. Hence, the necessity for a holistic approach for demand forecasting for the pharmaceutical supply chain has become imperative. Recently, soft computing techniques are being used widely for demand forecasting due to relatively higher accuracy compared to conventional statistical techniques. This work presents a comprehensive review on machine learning based models for demand forecasting in pharmaceutical supply chains. The performance parameters have also been discussed.

Keyword: *Demand Forecasting, Pharmaceutical Supply Chain, Soft Computing, Machine Learning, Mean Absolute Percentage Error (MAPE)*

I. INTRODUCTION

Due to the ongoing COVID-19 scenario, the pharmaceutical industry has witnessed extreme pressure in terms of delivering pharmaceutical products. Several instances have been encountered where life saving drugs and amenities fell short of demand causing -

extreme fatalities. Hence, it became evident that demand forecasting for the pharmaceutical supply chain was mandatory [1]. The pharmaceutical market is an important area of the country's economy, which must be given special attention due to the fact that it is one of the necessary factors for the timely provision of human health. Today, there are a large number of pharmaceutical products (medicines and equipment), which are mass-market goods by terms, the use of which can be divided into durable goods (for example, sanitation, hygiene, medical devices) and short-term use (medicines, medicine plant materials, medical cosmetics) [2]. The management became extremely hard-pressed in times of the pandemics due to the large variations and sudden up-surge in the demand for pharmaceutical products. The demand forecasting can actually be modelled as a time series given by:

ISSN : 2455-9679
SJIF Impact Factor : 6.008

$$Demand = f(time, assocauted\ attributes) \quad (1)$$

Here,
f denotes a function of.

The dependence of pharmaceutical demand over time makes it somewhat predictable under similar other conditions of global influencing variables. However, even the slightest of changes can derail the prediction completely.

II. NEED FOR SOFT COMPUTING FOR DEMAND FOREASTING

Primarily, soft computing based techniques are used where the data to be analyzed is extremely large and complex to be analyzed by conventional computational or statistical techniques. There are various soft computing based approaches used for time series prediction or fitting applications out of which neural networks and fuzzy logic have gained substantial prominence. With the advent of deep learning, the computational capability of algorithms have also risen allowing us to find trends in highly non-linear and uncorrelated data [3]. The following section briefly explains the fundamentals of neural networks and fuzzy systems and their application to stock market prediction.

2.1 Artificial Neural Networks (ANN)

Artificial Neural Networks try to copy or emulate the thinking process of the human brain to predict data. The fundamental properties are:

1) Parallel data processing capability
2) Learning and Adapting capability
3) Self-Organization

The mathematical model of ANN is shown below:

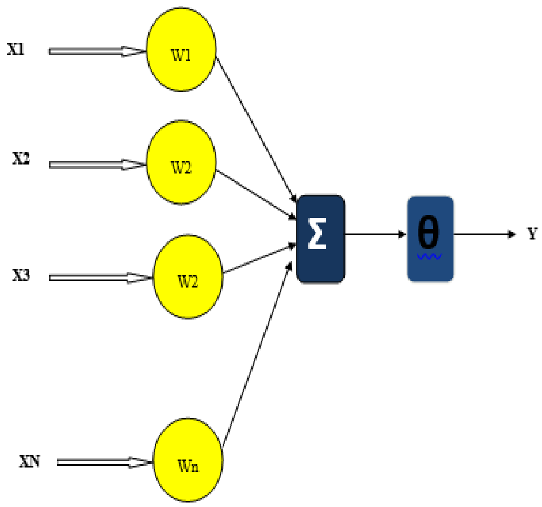

Fig.1 Mathematical Model of Neural Network

The output of the neural network is given by:

$$\sum_{i=1}^{n} XiWi + \Theta \quad (2)$$

here,

Xi represents the signals arriving through various paths,
Wi represents the weight corresponding to the various paths and Ɵ is the bias.

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The essence of neural networks lies in the fact that neural networks can find a relation among variables which may seem highly uncorrelated. Moreover, as the data keeps changing, the neural network structure keeps adapting in terms of the weights so as to optimize the model and reduce the errors in the output [4]. Fundamentally, the learning is sub categorized as under:

1) Computational Intelligence
2) Artificial Intelligence
3) Machine Learning
4) Deep Learning
5)

A set theoretic relationship among the above can be seen to be depicted by figure 2

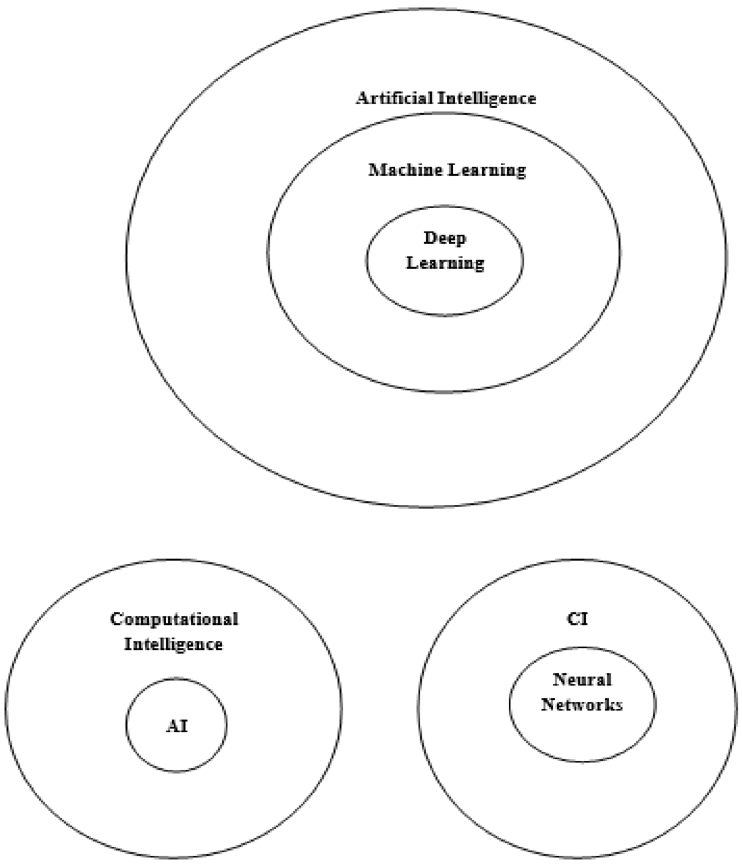

Fig.2 Relationship between machine learning paradigms

Moreover, neural network architectures are also categorized as:

Feedforward Networks: Feed forward networks consist of only the feed forward path for data to travel from input layer towards output layer

Recurrent Networks: Recurrent networks have at least one closed data path loop.

Back Propagation: Back Propagation feeds back the error at the output as an input

The diagrammatic representations are given below:

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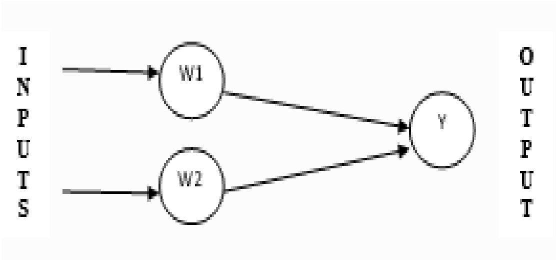

Fig.3 Single Layer Feed Forward Network

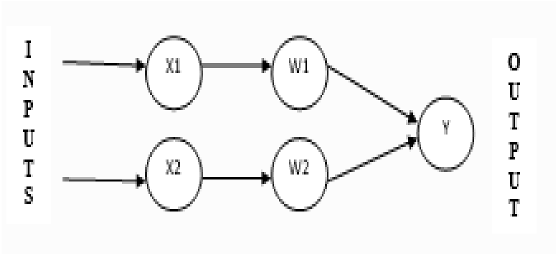

Fig.4 Multi-Layer Feed Forward Network

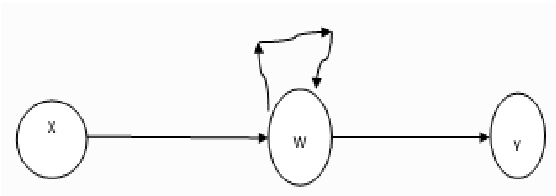

Fig.5 Recurrent Network

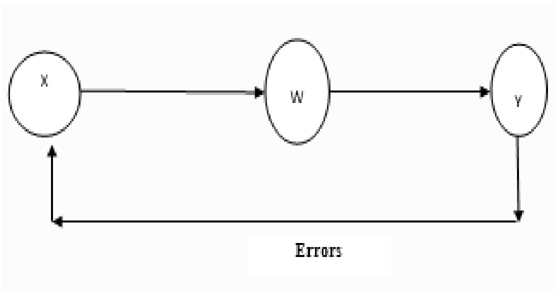

Fig.6 Network with back propagation

Out of the empirical neural network architectures, back propagation has gained significance due to its accuracy in prediction of time series applications. However the performance for different training algorithms vary considerably in terms of errors and number of iterations [5]

2.2 Fuzzy Logic

Another tool that proves to be effective in several prediction problems is fuzzy logic. It is often termed as expert view systems. It is useful for systems where there is no clear boundary among multiple variable groups. The relationship among the inputs and outputs are often expressed as membership functions expressed as [6]:

A membership function for a fuzzy set A on the universe of discourse (Input) X is defined as:

$$\mu A : X \rightarrow [0, 1] \qquad (3)$$

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Here,
each element of X is mapped to a value between 0 and 1. It quantifies the degree of membership of the element in X to the fuzzy set A.

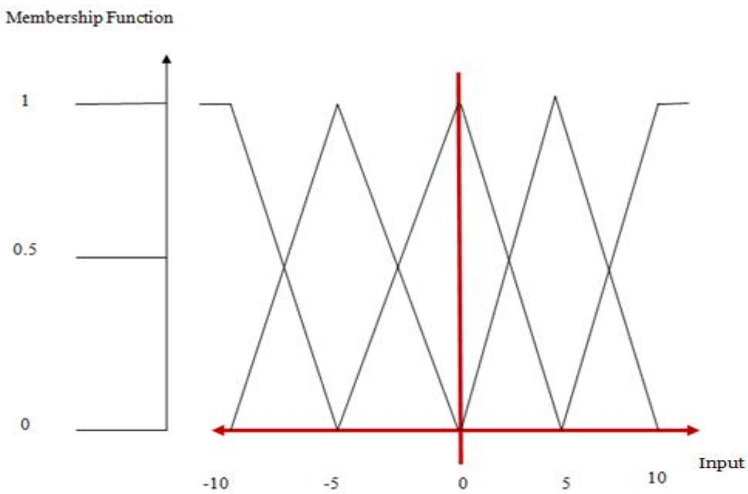

Fig.7 Graphical Representation of Membership Functions

Here,
x axis represents the universe of discourse (Input).
y axis represents the degrees of membership in the [0, 1] interval.
The final category is neuro fuzzy expert systems which governs the defining range of the membership functions.

2.3 Adaptive Neuro Fuzzy Inference Systems (ANFIS)

The ANFIS can be thought of as a combination of neural networks and fuzzy logic. In this mechanism, the neural network module decides the membership functions of the fuzzy module. The ANFIS structure is depicted in figure 8.

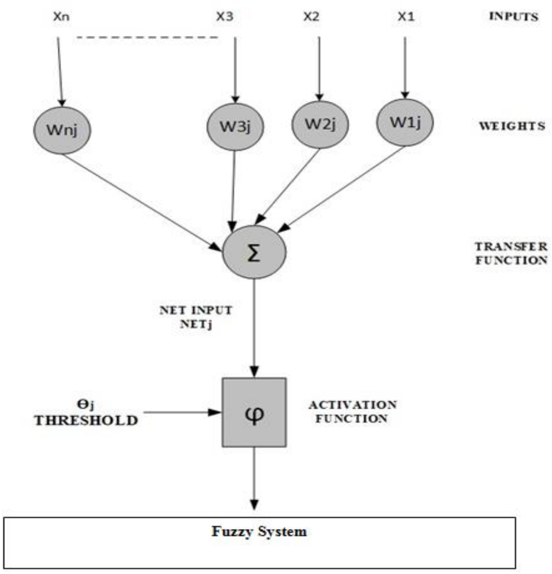

Fig.8 Block Diagram of Neuro-Fuzzy Expert Systems

III. Previous work

The survey of existing literature in the domain has been domain has been of extensive help in foreseeing the methodologies and gaps in existing work.

Oglu et al. in [1] proposed the use of fuzzy logic and a neural network to predict the demand for pharmaceutical products in a distributed network, in conditions of insufficient information, a large assortment and the influence of risk factors. A comprehensive approach to solving forecasting problems is proposed using: the theory of fuzzy logic - when forecasting emerging and unmet needs and a neural network - if there is a lot of retrospective information about the actual sale of drugs and drugs. Using this approach to solve the problems of forecasting demand allows you to get statistics and experience. The general algorithm, mathematical interpretation and examples of forecasting the demand for pharmaceutical products in the face of uncertainty of information are given, and the general structure of the system for forecasting the demand for drugs is described.

Fildes et al. in [2] showed that computer-based demand forecasting systems have been widely adopted in supply chain companies, but little research has studied how these systems are actually used in the forecasting process. Authors report the findings of a case study of demand forecasting in a pharmaceutical company over a 15-year period. Carrying out the judgmental interventions involved considerable management effort as part of a sales & operations planning (S&OP) process, yet these often only served to reduce forecast accuracy. This study uses observations of the forecasting process, interviews with participants and data on the accuracy of forecasts to investigate why the managers continued to use non-normative forecasting practices for many years despite the potential economic benefits that could be achieved through change. The reasons for the longevity of these practices are examined both from the perspective of the individual forecaster and the organization as a whole.

Goodarzian et al. in [3] showed that in the pharmaceutical industry, a growing concern with sustainability has become a strict consideration during the COVID-19 pandemic. There is a lack of good mathematical models in the field. In this research, a production–distribution–inventory–allocation–location problem in the sustainable medical supply chain network is designed to fill this gap. Also, the distribution of medicines related to COVID-19 patients and the periods of production and delivery of medicine according to the perishability of some medicines are considered. In the model, a multi-objective, multi-level, multi-product, and multi-period problem for a sustainable medical supply chain network is designed. Three hybrid meta-heuristic algorithms, namely, ant colony optimization, fish swarm algorithm, and firefly algorithm are suggested, hybridized with variable neighborhood search to solve the sustainable medical supply chain network model. Response surface method is used to tune the parameters since meta-heuristic algorithms are sensitive to input parameters. Six assessment metrics were used to assess the quality of the obtained Pareto frontier by the meta-heuristic algorithms on the considered problems. A real case study is used and empirical results indicate the superiority of the hybrid fish swarm algorithm with variable neighborhood search.

Amalnick et al. in [4] proposed an accurate demand forecasting in pharmaceutical industries has always been one of the main concerns of planning managers because a lot of downstream supply chain activities depend on the amount of final product demand. In the current study, a five-step intelligent algorithm is presented based on data mining and neural network techniques to forecast demand in pharmaceutical industries. The main idea of the proposed approach is clustering samples and developing separate neural network models for each cluster. Using the obtained data, the performance of the proposed approach was assessed in a pharmaceutical factory. The optimal number of clusters for this case was four. Mean arctangent absolute percentage error, average relative variance, and correlation coefficient (R) were used to evaluate the performance of different neural network structures. The results of performing the models once for all data and once for the data of each single cluster showed that the forecasting error significantly decreased thanks to using this approach. Furthermore, the results indicated that clustering products not only raises the prediction accuracy but also enables a more reliable assessment of forecasted values for each single cluster. Such analyses are

ISSN : 2455-9679
SJIF Impact Factor : 6.008

very important and useful for managers of marketing and planning departments in pharmaceutical units.

Viegas et al. in [5] showed that The Pharmaceutical Supply Chain (PSC) is responsible for considerable environmental and product-value impacts. However, studies on the reverse flows of PSC do not capture the diverse routes of end-of-use and end-of-life medicines (EOU/EOL-M) and how the constraints in the forward supply chain processes and operations impact such reverse flows. This research proposes a classificatory review in which three categories of reverse flows are identified: donations, Reverse Logistics (RL) and Circular Economy (CE). Donations are characterized by explicit philanthropic acts involving corporate reputation or by emergency humanitarian action. RL is boosted by regulatory issues and restricted by business imperatives of the PSC. CE is characterized by informal loops of not expired medicines, mainly due to health professionals' initiatives (although this may not be clear to participants). This classification emerged from content analysis of 2622 references found in six databases, from which 127 were selected.

Chen et al. in [6] consider a pharmaceutical supply chain composed of one pharmaceutical manufacturer and one pharmacy. Authors investigate how price cap regulation affects pharmaceutical firms' pricing decisions. It also evaluates the economic and social performance of the pharmaceutical supply chain and assess the risks associated with price cap regulation. The derived equilibriums under different price cap regulations, including retailer price cap regulation, manufacturer price cap regulation and linkage price cap regulation, are compared to that without regulation. The results show that one-sided price cap regulation will damage the economic performance of the regulated firm, whereas the unregulated firm may gain a financial advantage. The regulation may increase the risk of a supply shortage if pharmaceutical firms cannot cope with the financial loss. In contrast, linkage price cap regulation can be an effective policy for improving both the economic and social performance of the pharmaceutical supply chain.

Balashirin et al. in [7] showed that Researches confirm that the area that has the greatest reimbursement of outlays on economic development is a higher education, and that is the reason why the formation of a financial policy in the area of higher education is of utmost importance. Improving the quality of higher education and promoting its welfare in the economy, the socioeconomic governance indicators will also improve. The authors proposed a neural network model for the estimation of impact of financing policy on socio economic and socio educational system.

Ahmadi et al. in [8] showed sustainable development of a nation greatly depends on the health of individuals. The emergence of the diseases caused by unhealthy lifestyle as well as the growth and aging of the population have faced the pharmaceutical industry with an increasing demand for drugs and the related products over time. This increase in demand has made the pharmaceutical industry as an important and large industry which constitutes a considerable portion of the healthcare expenditures. This sector is grappling with many challenges and inefficiencies in research and development activities, introducing new products, procurement, manufacturing, storage, and distribution affairs. Such issues have resulted in the inability of pharmaceutical companies to satisfy market demand in an efficient while effective manner. These problems alongside the dynamic and complex nature of a pharmaceutical supply chain (PSC) necessitate the employment of efficient optimization techniques to provide these companies with informed decision making by relying on available data. Hence, this chapter aims to identify the prevalent challenges of PSCs at three different decision levels, i.e., long-term (strategic), mid-term (tactical), and short-term (operational) decisions; as well as presenting various ways to deal with such problems. Accordingly, first, the characteristics of a PSC are presented and discussed. In order to provide a tangible perspective for application of Operations Research in PSC, an exhaustive mathematical programming model is presented.

Sabouhi et al.in [9] present an integrated hybrid approach based on data envelopment analysis (DEA) and mathematical programming method to design a resilient supply chain. First, the efficiency of potential suppliers is evaluated by a fuzzy DEA model. Afterwards, using the obtained efficiency, a two-stage possibilistic-stochastic programming model is developed for integrated supplier selection and supply chain design under disruption and

ISSN : 2455-9679
SJIF Impact Factor : 6.008

operational risks. The model incorporates partial and complete disruptions of suppliers as well as quantity discount for procurement of various raw materials. Furthermore, we utilize several proactive strategies such as fortification and pre-positioning emergency inventory at fortified suppliers, and using multiple sourcing to enhance the resiliency of supply chain. Atra pharmaceutical company (APC) is used as a case study to investigate the applicability of the proposed model and analyze the solution results. The results indicate the validation of proposed model and the impact of various resiliency strategies.

Settanni et al. in [10] evaluated the evaluates reconfiguration opportunities in Pharmaceutical Supply Chains (PSC) resulting from technology interventions in manufacturing, and new, more patient-centric delivery models. A critical synthesis of the academic and practice literature is used to identify, conceptualise, analyse and categorise PSC models. From a theoretical perspective, a systems view of operations research is adopted to provide insights on a broader range of OR activities, from conceptual to mathematical modelling and model solving, up to implementation.

IV. Performance Metrics

The performance metrics for the evaluation of the forecasting models are presented here:
Mean Square Error:
It is mathematically defined as:

$$mse = \frac{1}{n}\sum_{I=1}^{N}(X - X')^2 \qquad (8)$$

Here,
X is the predicted value and
X' is the actual value and
n is the number of samples.

Mean Absolute Percentage Error (MAPE)
It is mathematically defined as:

$$MAPE = \frac{100}{M}\sum_{t=1}^{N}\frac{E - E_t|}{E_t} \qquad (8)$$

Here,
E_t and E_t˜ stand for the predicted and actual values respectively.

Iterations:
The iterations denote the number of cycles of training needed to reach convergence.

V. Conclusion

Off late, the demand for pharmaceutical products and drugs has ramped up significantly due to the ongoing COVID-19 scenario. Several instances have been reported where large scarcity of drugs have led to fatalities in patients. Hence, the necessity for a holistic approach for demand forecasting for the pharmaceutical supply chain has become imperative. Recently, soft computing techniques are being used widely for demand forecasting due to relatively higher accuracy compared to conventional statistical techniques. The demand for pharmaceutical supplies are dependent on several parameters which are extremely intermittent in nature and techniques which are capable of handling intermittently volatile datasets are to be used for their analysis. The review of the existing benchmark techniques paves the path for further research in the domain.

ISSN : 2455-9679
SJIF Impact Factor : 6.008

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