Post COVID-19 Supply Chain Optimization for the Indian Pharmaceutical Industry using AI Techniques

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The COVID-19 pandemic has overwhelmed healthcare systems around the globe, having an indirect effect on the treatment of other diseases. During these unprecedented times the Indian pharmaceutical industry has been busy responding to all the sudden healthcare challenges that were arising from the disruption in supply chains, and this has showcased a necessity to improve functioning of the industry. Overall, India is one the fastest emerging pharmaceutical markets but many faults from the past decade in the Indian supply chain system have been highlighted by this pandemic. This paper discusses the critical elements of any supply chain and the various strategies that a pharmaceutical company can use to function efficiently. Some of the more modern approaches used by companies are artificial intelligence (AI) and machine learning (ML) tools in supply chain optimization. These new technologies help reduce lead times, significantly lower costs and help predict better routes for the future. The paper then analyzes an active pharmaceutical ingredient (API), paracetamol which is a highly produced drug in India. Evaluating its current production in the supply chain process, the paper suggests ways to improve supply chain for this particular API in India. All in all, improving the supply chain management in India by developing coherent strategies and making data-driven decisions has the potential to improve organizational profitability.

Introduction

The outbreak of COVID19 has caused instability in the entire world in all aspects of life. From unprecedented challenges to public health to millions of industries facing existential threats, this pandemic has devastatingly disrupted our economic and social systems. (*Impact of COVID-19 on People's Livelihoods, Their Health and Our Food Systems*, n.d.) In particular, it has caused a major disruption in various supply chains which has forced many companies to reconsider their existing strategies, specifically their dependency on imports from other countries. India is one of those countries which have been gravely affected by the pandemic in terms of economy, life, and healthcare. India has a very large healthcare sector and is slowly emerging to become "the Pharmacy of the World." (*India's Reputation as Pharmacy of World Reinforced*, 2021) However, over the years, India has become significantly dependent on the import of basic raw

materials from foreign markets which are then used to manufacture finished dosage formulations and ready for patient use. Even though there has been a rapid global growth in the healthcare sector for APIs around the import of raw pharmaceutical industries from emerging markets, India's increasing dependence on China for many APIs has been a constant growing concern for this sector.

Supply chains deal with the whole process of production, starting with the primary suppliers of raw materials and reaching the equipment of the final factory where products are made. Raw materials and intermediate products are also transported across different factories as transitional steps in the supply chain process. Therefore, transportation also plays a big role in supply chain management (SCM). Eventually, after the final product is manufactured and packed, it is distributed to different buyers to fulfill their demands. This is an extensive and tedious process that is susceptible to disruptions if even one element of the chain is broken. COVID19 demonstrated exactly this. During this period the demand for medicines increased due to higher demand of pain relief tablets for COVID19 patients. As a result, the pharmaceutical industry in India could not fulfill the demands of its people due to insufficient production from an unavailability of raw materials.

This paper analyzes the Indian pharmaceutical industry and discusses challenges within the country's supply chain management as well as investigates potential improvements to better manage unforeseeable situations like COVID19. Tougher environmental controls and regulations have also forced companies to rethink their strategies regarding their supply chain approach. On a more general note, this review suggests implementing new practices like data integrity and improved inventory management across all supply chains so that major disasters in the supply chain management of pharmaceuticals can be avoided and companies can easily keep up with both, domestic and global demand. Specifically, AI and ML can bring exceptional value to logistics and supply chain. As the COVID19 crisis continues to evolve, companies all over the world are striving to respond and create a fast, efficient, and nimble supply chain to mitigate risks. In order to achieve this goal, companies must harness the power of technologies like AI and ML to generate insights which improve decision making. From cost saving to risk mitigation to more optimized routes, AI has numerous applications in each stage of supply chain management.

The Indian Pharmaceutical Industry and its Big Players

According to the Indian Economic Survey of 2021, India's domestic pharmaceutical market is estimated at 42 billion USD. Additionally, India's drug and pharmaceutical exports were 17.57 billion USD from December, 2020 to April, 2021. (*Pharma Industry in India: Pharma Sector Overview, Market Size, Analysis...| IBEF*, n.d.) The swiftly rising presence of India in the global pharmaceutical industry can be seen in its 20% share in global supply by volume and a 62% share of global demand in vaccines. It is the largest supplier of generic

medicines worldwide and is placed third for production by volume. The main features of this industry include having a market growth rate of about 10-12% a year and a 33% less manufacturing relative to western markets. (*Pharmaceutical Industry in India*, n.d.) Figure 1a illustrates a representation of India's global exports. Here, in terms of value, the United States has the highest share of about 5.2 billion USD, China being the second is valued at 2.3 billion USD and the third highest being United Arab Emirates is 1.3 billion USD in terms of values exported.

During the pandemic, the Indian government started a 2 billion USD program to enhance the 'make-in-India' product development which sought to import substitution, which is the concept of blocking imported manufactured goods in order to boost the economy by increasing the demand for domestically produced goods, and improve local production of active pharmaceutical ingredients (APIs). (*Cabinet Approves Production Linked Incentive Scheme for Pharmaceuticals*, n.d.) Owing to India's large and capable pool of scientists and engineers, this country has the potential manpower to steer this industry to greater heights. Within India, the major pharmaceutical hubs are Ankleshwar, Vadodara, Vapi, Kolkata, Hyderabad, and Mumbai. The major pharmaceutical companies of India are listed in Figure 1b. It is visible that these companies have a large market capitalization which competes with the largest companies worldwide in their respective products. Altogether, this shows that India is a major player in the pharma industry globally.

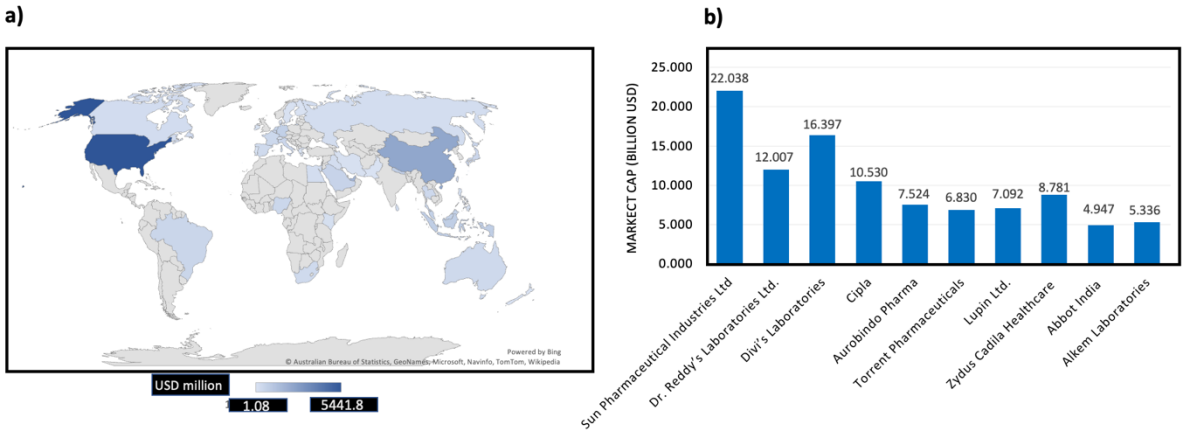

FIGURE 1. India's global exports and major companies a) The value of exports of pharmaceuticals from India to different parts of the globe; b) Top 10 pharmaceutical companies in India and their market capitalization.

India's Dependency on China for Raw Material

India is majorly dependent on China for raw materials like API intermediates for the manufacturing of different pharmaceuticals. Compared to domestically producing APIs, importing produced APIs from China decreases costs by 20-30%. This cheap labor from China is a result of aggressive government support programs, subsidized

interest, and free land that have lowered the cost of APIs in China by over 40%. (Magazine, Monday 19 July 1:43) Furthermore, in India, the relaxation of license policies and execution of the 2005 product patent law, which defines what an invention is and makes it clear that any existing knowledge cannot be patented, caused pharmaceutical players in India import APIs rather than produce them domestically. Thus, India imports around 80% of its required APIs and intermediates, creating a strong dependency that has lasted for years.

In order to be more self-reliant, India adopted the production linked incentive (PLI) scheme, in March 2020, for the advancement of local manufacturing of drug intermediates and key starting materials. Additionally, the country instituted a scheme for promotion of bulk drug parks wherein infrastructure is initiated for bulk drug production units. (*Schemes For Promotion of Pharmaceutical Industry | Make In India*, n.d.)

Need for a Good Supply Chain Management and how India can Benefit from it

A supply chain consists of dealing with the conversion of raw materials into finished goods and the convenient delivery of products at the end. The three main elements of the supply chain are the retailer, the manufacturer, and the supplier who are involved in providing products to their customers. (Parkhi, 2015) Good SCM in the pharmaceutical industry can modernize a company by making better use of assets and funds available to positively respond to customer demand. Good management is needed for efficiency which subsequently affects all business processes such as data accuracy, reduction of complex operations, supplier selection, and buying and distribution. (Kapoor, 2018) Figure 2a shows the different applications of ML algorithms in SCM including sales forecasting, logistics planning, inventory optimization etc. With versatile applications, these tools can be used to improve the overall working of the supply chain.

Good SCM also reduces operating cost by creating networks that can meet customer demands at a much more affordable rate. Effective SCM ensures that raw materials consistently arrive at manufacturing production plants on time, thereby preventing the need to outsource these materials from an alternative source saving both, valuable time and money. In this way it boosts profits of an organization. Visibility is achieved by knowing where the particular inventory is at a particular time, and how well products in transit can be traced. Efficiency is also attained by improving planning of operations and making maximum use of resources whether they are financial, human, technological or physical. (Singh et al., 2016) To conclude, good SCM can be achieved via control of product, shipment, and distribution.

Figure 2b highlights the major challenges in the Indian pharmaceutical industry.

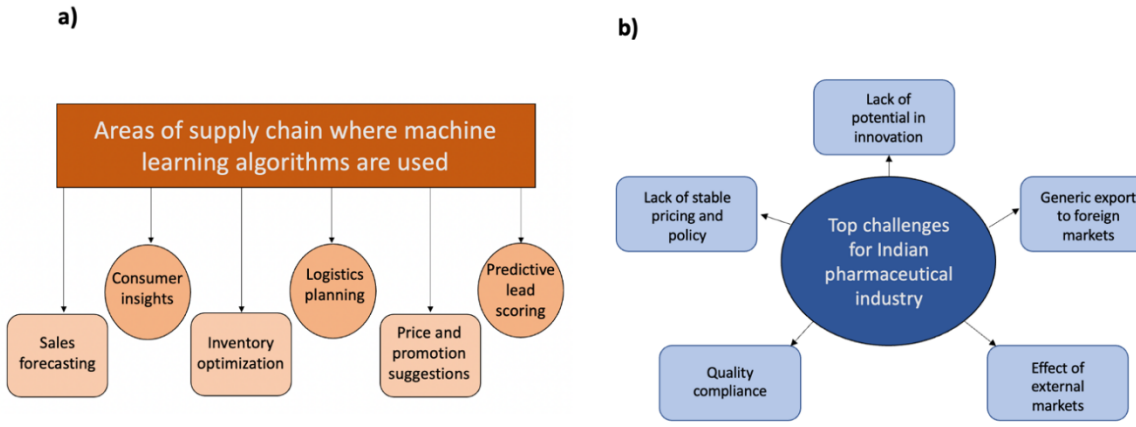

FIGURE 2. The challenges and methods of improvement in SCM a) Highlights of the applications of machine learning tools in supply chain management b) Top challenges in supply chain management for the Indian pharmaceutical industry.

With focus on the large scale of this industry in India, this paper goes on to highlight the major challenges within Figure 2b faced within the Indian pharmaceutical industry and its corresponding SCM. ('Indian Pharma—Some Challenges and Acceptances', 2020)(Jayapala Reddy & Rao, 2017) According to the Indian Pharmaceutical Alliance (IPA), there are existing problems hindering the progress of pharmaceutical organizations. Out of all the barriers, a "lack of stable pricing" and "lack of potential in innovation" are more prevalent in India than in any other country. The following points are some of the major challenges and roadblocks the Indian pharmaceutical industry faces:

1. *Lack of potential in the innovation space*: despite being rich in personnel and talent, the Government of India lacks in its investment in research, development, and innovation. These are all necessary assets to refine in order to grow this sector further in India. The government must finance and encourage clinical trials for new methods.
2. *Generic export to foreign markets*: The Indian pharmaceutical market is starting to decrease because of buyer consolidation and higher competition. Due to price weakening, exports to the United States have started to flatten, whereas previously exports had been increasing.
3. *Effect of external markets*: Indian markets are still heavily reliant on Chinese raw materials, intermediates, and APIs for the manufacture of their products due to their lower costs. Factors such as unpredictable price fluctuations of these products give China the upper hand, and this has a looming effect over the pharmaceutical sector in India.
4. *Inquiries of quality compliance*: A lot of capital is used up in quality checks and health inspections. Since 2009, India has undergone the highest number of Food and Drug

Administration (FDA) inspections causing capital to be used in this field instead of areas such as research and innovation.

5. *Lack of stable pricing and policy*: Frequent fluctuations in domestic pricing and change in policies in India create an unclear environment for investors and innovation.

Improving speed to the market by increasing agility and logistics can help overcome many of these challenges. The final purpose of the SCM is to obtain value for customers and an efficient supply chain network. Supply chain entities must unify their inter and intra organizational processes. The policies recommended in a study by Moosivand et al. can lead to the pharmaceutical supply chain to be more consolidated. (Moosivand et al., 2019) This can lead to overcome some of the challenges mentioned above.

Strategies and Elements to Improve Supply Chains in India

In order to overcome the different challenges in the supply chain in India, it is crucial to improve current operating strategies which lack efficiency and innovation to be a step above in this extremely competitive market. Here, the paper discusses the elements needed for any good supply chain along with showcasing new strategies to improve it within the Indian pharma sphere. It is well-known that organizing and developing a steady supply chain takes years of a united effort, particularly within the pharmaceutical industry where intermediates are often shipped around the globe until the final product is obtained. Particularly, India lacks innovation potential which can also be enhanced by AI by providing managers with critical information to make more informed decisions regarding new technologies and innovations. Companies must perceive the power of information technology (IT), and collaborate it with their business alliances.

B.S. Reporter reported that about 15-20% of the production capacity could be increased through different initiatives such as reducing lead times, quality check turn-around times, and changeovers. (Reporter, 2020) In order for any organization to function at its optimum level, this 15-20% gap must be reduced to ensure overall progress. Inventory management is very crucial as there should be sufficient inventory to fulfil demands but simultaneously does not over-anticipate sales (which would result in excess inventory). Especially for new products where the demand is relatively unknown, a proper strategy must be put into place to manage inventory by first studying the demand and application of the product in detail. In addition to this, an organization must have a proper packaging strategy especially because certain products which are susceptible to environmental change must have appropriate containers for them to be shipped. Time intervals can also be reduced with faster and more efficient packing. (*8 Critical Elements Of A Supply Chain Strategy — From Discovery To Commercialization*, n.d.) Figure 3 shows the pathway of SCM in the pharmaceutical industry depicting what all the raw materials undergo before being converted to finished goods and

being distributed. These methods will help a company have an efficient strategy in order, which will improve the overall supply chain.

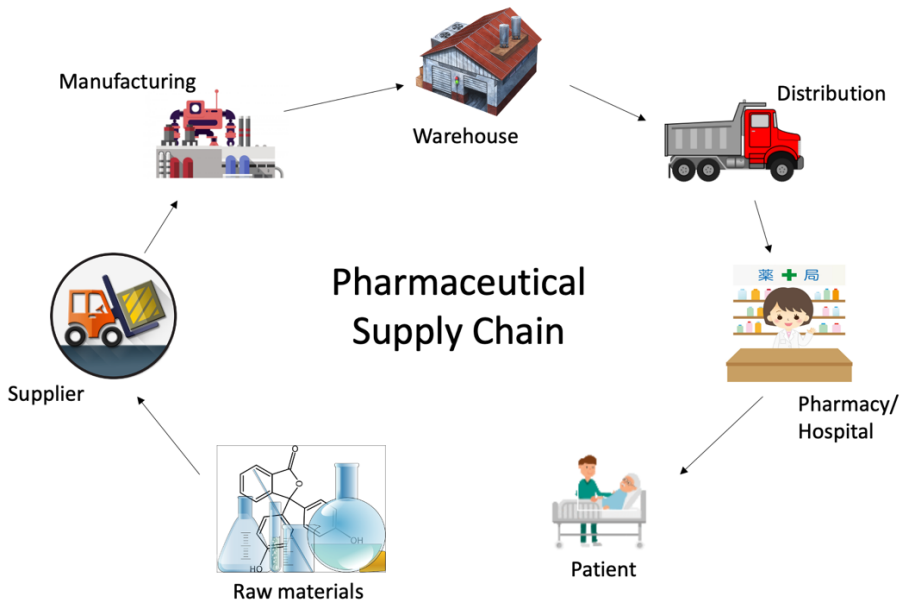

FIGURE 3. Entire process of supply chain management for a pharmaceutical company. The process starts with the acquirement of raw materials which undergo manufacturing to form the desired product which are then delivered to the customer.

Artificial Intelligence (AI) and Machine Learning (ML)-driven Supply Chain Optimization

The constant growth of the pharmaceutical industry has led to the invention of novel technologies to improve SCM, one of which is using AI. While AI refers to many automated algorithms, its main goal is the simulation of human intelligence by computers. These systems work by acquiring and ingesting large amounts of already available data, analyzing patterns and trends, and then making predictions on unseen data. ML is a sub-category of AI and computer science which allows systems the ability to automatically learn, understand, and improve from experience without explicitly being programmed. Machine learning models are excellent in at analysing trends, spotting anomalies, and predicting future trends with large data sets. Hence, ML is extremely useful in managing suppliers and documentation, planning the movement of goods, and forecasting likely demand from suppliers.

The pandemic has shown that it is imperative for companies to get drugs and vaccines to the market as soon as possible. AI has the potential to both foster innovation and enhance productivity, giving better results across the supply chain. AI can also drive innovation by creating new business models. Here, this paper explains relatively new technology that can be applied not only in the supply chain in the pharmaceutical industry but also the value chain, which is a business model that describes the full range of processes needed to create a

product, right from drug discovery and development to production and marketing.

In order to overcome the above-mentioned challenges like logistic costs, high working prices, and quality control an increasing number of companies are beginning to adopt AI which have shown improved success rates in the generation of more affordable drugs, reduced working prices, and simplifying the drug delivery process. Particularly, an approximation by the International Business Machines corporation (IBM) shows that the entire healthcare sector has around 161 billion gigabyte (GB) of data (as of 2011). (Krishnaveni et al., 2020) With this enormous amount of data available, AI can be of great help in analyzing data and predicting results that would make the decision-making process easier thereby improving overall functioning of the organization.

AI also promises the potential to reduce logistics costs by finding patterns in all the data collected over the years. Along with this it can detect inconsistent supplier quality levels and delivery performance giving information on who the best and worst suppliers are. Currently, a lot of inspections are automated, and the results obtained are uploaded on a cloud-based platform. These cloud based platforms have several disadvantages like risk of data confidentiality, greater communication time, and poor connection when the server is down. (Alhadawi et al., 2017) Machine learning technologies have algorithms that can reduce risks and potential frauds. (Columbus, n.d.) Even more than cyber security, ML tools predominantly focus on matters related to fraud detection and suspicious transaction detection. For example, in the paper by Villalobos and Siva, a C.50 algorithm was applied to predict risk levels based on various general customer probable risks to determine the relative importance of each. These key factors were used to characterize transaction profiles. After testing, this model provided a 99.6% correct classification rate and the number of alerted cases were reduced from 30% to under 1%. (Leo et al., 2019)(Villalobos & Silva, n.d.) Conventionally, pharma companies do not spend a lot of their finance, resources or time on looking for treatment for rare diseases because typically the return on investment (ROI) is extremely low as compared to the time, and effort it takes to develop a cure. AI can however, significantly cut down the time factor to gather information for the treatment of a rare disease and, can potentially be easily incorporated into pharma companies with the correct investment.

Another important and relevant use of AI and ML is in helping predict an epidemic. Many companies use these resources to forecast epidemics across the globe. Technologies feed on available data from various sources and in accordance with geological, environmental, and biological components in an effort to connect the datapoints and predict an epidemic. A paper by Feng et al discusses different models to predict epidemics. One of these models is called Susceptible-Exposed-Infected-Removed (SEIR) model. Specifically, this paper collected COVID-19 data of people in China consisting of those cases confirmed, cured, and died from January 23 to March 6, 2020. As a result, the SEIR model could quite effectively predict the epidemic

situation, and the AI model which added migration statistics could predict a similar situation in non-Wuhan areas in China. (Feng et al., 2021)

AI can furthermore be used to control and improve portions of the manufacturing process of drugs in the form of design optimization, process automation, and quality control in response to an oncoming epidemic. Due to this, drugs can be launched in the market much quicker and at lower costs.

Companies can also build a supply chain predictive model that can automatically analyze the best routing alternatives for raw material supply chain. Machine learning models can be used to feed supply chain data such as transportation rates as well as policies and data concerning shipping routes etc. The different applications of AI in transport include: (Conde & Twinn, n.d.)

1. Traffic management operations – Many cities around the globe have started using AI to help solve traffic jam problems. For example, Bengaluru, India has fairly common traffic jams. To counteract this problem, Siemens mobility has built a monitoring system which uses AI through the means of traffic cameras that calculates the traffic density by detecting vehicles and manipulates traffic lights based on the traffic on the roads.
2. Aviation – Sichuan Tengden Technology is a Beijing based startup that has developed a drone which is capable of carrying up to 20 metric tons of load and can fly as much as 7500 kms. This is just one of the many applications for AI technologies in drones. ML can provide the ability for drones to study existing data and perform tasks like landing with autopilot or flying to an already known location.
3. Logistics – The use of AI and ML can make the customs process much easier. For example, a Mexican company called Logiety applies ML tools to streamline the international customs and by classifying and segregating products for import-export on the basis of material and size. These are them matched with their respective tariffs.

With an increase in AI and navigation technologies an organization can make great use of simultaneous localization and mapping of raw materials or final products when they have been shipped. It can help a company by following customer journeys and showing them which marketing technique has led customers to purchase from them. This allows companies to predict success or failure rates of different campaigns. (*Artificial Intelligence in Pharmaceutical Industry*, 2021) In this way, both the buyer and seller can have all information about the product since all the processes are in automation. Right from the moment a product is bought, the buyers directly communicate to virtual assistants or chatbots. The AI system thereafter responds to any requests or queries related to procurement, transaction and payment. This significantly reduces time and money since less manpower is needed. Even if invoices are submitted late, the

AI system will trigger an internet search for a red flag that might indicate internal problems at the supplier end. [26] Many major international companies such as Roche, Pfizer, Merck and, Johnson & Johnson have already acquired AI technologies. (PharmaNewsIntelligence, 2021) Indian companies too should follow such approaches for better results in management of their supply chain.

Finally, AI and ML tools have also demonstrated their potential role in predictive chemistry and synthetic planning of small molecules. This technology can be used to solve any challenge related to complex biological networks such as recognizing what drug composition would be best suited for treating certain aspects of a particular disease. In fact, research and development (R&D) is considered as the preliminary step of SCM. R&D decides which processes will be used and which raw materials will be needed. Thus, any organization must cooperate in R&D investment and then decide the production quantity according to a wholesale cost contract. (Ge et al., 2014) For chemical synthesis, the main aim is to generate methods of synthesis that are more cost effective, diverse, and accurate. However, the application of AI and ML is only possible through data which is already available. The predictive power of AI mainly depends on data diversity and if the available training data does not cover all aspects of chemical subparts, AI application in chemical synthesis routes will be limited. A solution is using the database of chemical compounds and sequences held by the Chemical Abstracts Service (CAS), a branch of the American Chemical Society. CAS reactions offer the data needed to improve the predictive power of synthesis organization. This database has collected data for more than 10 years which covers detailed information from patents, journals, and publications all over the world. In partnership with Bayer, CAS has set up a machine learning training set which was fed with CAS data which improved predictive power. A study was conducted on this which revealed that even a medium sized set of data from CAS reactions can remarkably improve the power of synthesis planning tools. The effect of this was just seen over a small section of reactions which suggest that even better predictive powers could be seen, were the training sets to be larger and of better quality. This proof of concept has vast applications in synthesis routes of small molecule drugs. Results from this study showed that the addition of reactions from the CAS database improved the accuracy from 16% to 48%. (*Find a Better Route*, n.d.) Figure 4 illustrates how AI and ML have a positive impact on supply chain optimization by reducing the chances of human error, storing, and applying large amounts of available data to forecast trends in the market and optimize route planning.

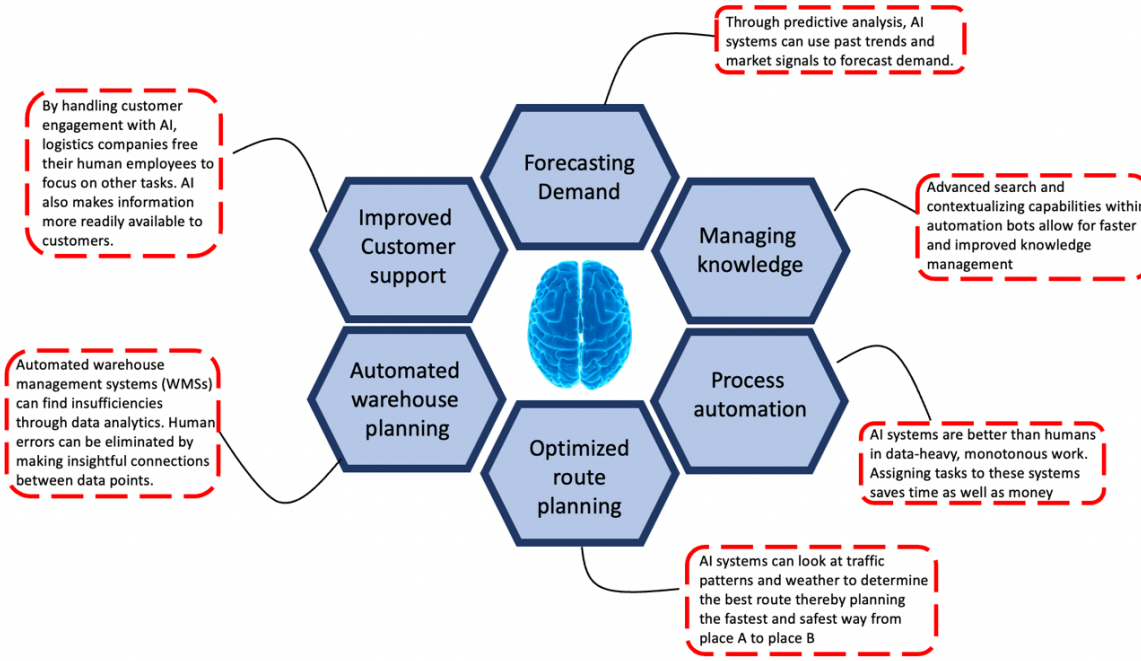

FIGURE 4. Various AI techniques used for supply chain management which can be implemented by companies for greater efficiency.

In-depth Analysis of Paracetamol Synthesis

This section focuses on supply chain optimization of the paracetamol synthesis process, a pharma pipeline very common in India that can benefit from improvements in the SCM. Ways to improve these routes for industrial manufactures in India are elucidated. Also known as acetaminophen, paracetamol is a synthetic non opioid derivative of *p*-aminophenol used for the treatment of cold and flu. Its effects generally last about two to four hours and causes much less damage to the liver as compared to aspirin. (*Production of Paracetamol (Acetaminophen).Pdf*, n.d.) The main manufacturers of paracetamol in India, in order of production volume, are Farmson Pharmaceuticals, Meghmani LLP, Sri Krishna Pharmaceuticals, Granules India Ltd, Bharat Chemicals, and Para Products Pvt Ltd. (www.tofler.in, n.d.)

There are different industrial ways of preparing paracetamol. The main raw materials are phenol, nitrobenzene, *p*-nitrocholoro benzene along with different catalysts, acids, and others.

Synthesis of Paracetamol

There are over 300 synthesis paths that could potentially form paracetamol. Nonetheless, the most commercially feasible routes are the ones that rely on petrochemical feedstocks derived from benzene such as phenol, nitrobenzene, and *p*-nitrocholoro benzene. Regardless, the starting material needed is phenol. There are three main industrial routes to prepare paracetamol:

1. The first one uses phenol as the starting material which is nitrated to give *ortho* and *para* toluene. *Ortho*-nitro toluene is removed by steam distillation leaving the *para* isomer which

is reduced in the presence of sodium borohydride to a *para*-amino group. This *p*-amino group is then acylated to give paracetamol.

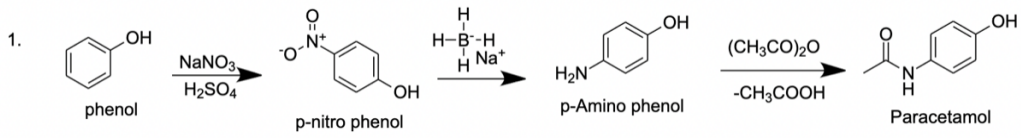

FIGURE 5.1. Route 1 of synthesis of Paracetamol.

2. The second route starts with phenol and, similar to the first route, is nitrated to give *ortho* and *para* toluene. *Ortho*-nitro toluene is removed by steam distillation leaving the *para* isomer which is reduced in the presence of sodium borohydride to a *para*-amino group. The only difference lies in the final stage where *p*-Amino phenol is acylated by acetyl chloride instead of acetic anhydride to give paracetamol.

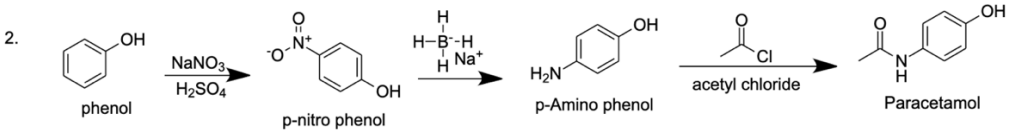

FIGURE 5.2. Route 2 of synthesis of Paracetamol.

3. Lastly, the third route starts with phenol as the starting material and is more popularly called as Hoechst-Celanese process. It involves two major steps. In the first step, *para*-hydroxyacetophene reacts with hydroxylamine salt in a base to give *para*-hydroxyacetophenone oxime. Then, this oxime is treated with a Beckmann rearrangement catalyst. From this, *p*-aminophenol is obtained which is filtered and dried. It is then reacted with acetic anhydride to produce paracetamol. (*Production of Acetaminophen - Patent US-5155273-A - PubChem*, n.d.)(Friderichs et al., 2007)

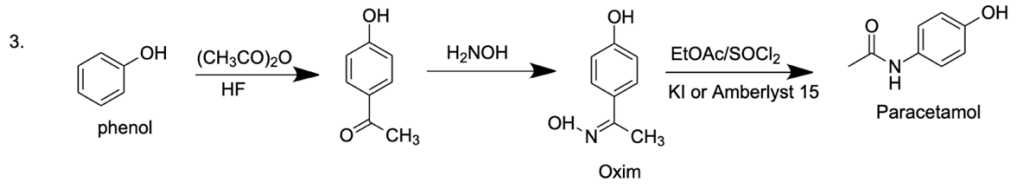

FIGURE 5.3. Route 3 of synthesis of paracetamol, Hoechst-Celanese process.

SYNTHESIS PROCESS	INTERMEDIATE STEPS	AE* %	YIELD %	RAW MATERIALS	PRICE (USD PER KG)	PRICE (USD PER KMOL)	ECO SCALE SCORE
ROUTE 1	Nitration of phenol	50	37	1.Phenol 2.Sodium Nitrate 3. Dil. Sulphuric acid	1. 1.00 2. 0.20 3. 0.26	1) 94.11 2) 17.00 3) 25.68	-
	Reduction	62	74	Sodium borohydride	0.80	30.40	-
	Acylation	72	60	Acetic anhydride	1.50	153.00	-
	Overall	36	16			337.19	43.00
ROUTE 2	Acetylation	81	99	Acetyl chloride	3.00	235.50	-
	Overall	38	27			419.69	46.50
ROUTE 3	Acetylation of phenol	88	96	Acetic anhydride	1.50	153.00	-
	Oximation	63	99	Hydroxyl amine	10.00	330.00	-
	Rearrangement	100	71				-
	Overall	58	68			482.98	60.00

TABLE 1. Comparison of different synthetic routes towards paracetamol with respect to yield %, atomic economy % and raw materials used and their Eco Scale scores(* AE- atomic economy which is the molecular weight of isolated product divided by sum of molecular weights of reactants (Vanden Eynde, 2016) *(*Phenol, China Phenol, Phenol Manufacturers, China Phenol Catalog*, n.d.)*)

Table 1 summarizes the three routes of industrial paracetamol synthesis in terms of the % yield, % atomic economy, raw materials used, and price. The first route is the most common and conventional route used. The cost of paracetamol through this route is 2.23 USD per kg. Despite being the cheapest route, Paracetamol gives a yield of only 16%. The second route can be used if there is any shortage in acetic anhydride. Although acetyl chloride is twice the price of acetic anhydride it gives a slightly better yield of about 27%. This is because acid anhydrides tend to be less electrophilic than acyl chlorides and only one acyl group is transferred per molecule of acid anhydride, which leads to a lower atom efficiency. (*Reactivity of Anhydrides*, 2013) For supply chain management, it is important for acetic anhydride or acetyl chlorides to be stored in glass carboys and transported in a cool, dry, and well-ventilated environment. In 1990, a patent was granted for a new process to manufacture paracetamol called the Hoechst Celanese process, or route three. (*Production of Acetaminophen - Patent US-5155273-A - PubChem*, n.d.) This process gives a much greater yield of 68%, however, at a higher manufacturing cost due to the hydroxyl amine group used in the oximation reaction.

The Eco Scale

To determine the overall greenness of a chemical reaction many factors like price, easy, safety and handling, renewability, and toxic emissions must be taken into consideration along with the mass balances. Calculations of energy used in reaction as well as energy used to extract, recycle, or destruct reagents or solvents must also be taken into account. Therefore, a "life cycle analysis" must be conducted and the principles and structure of this is given in ISO 1404:2006 document. (*ISO 14040:2006(En), Environmental Management—Life Cycle*

Assessment—Principles and Framework, n.d.) However, since this is very complex, another method is developed by Van Aken et al. only takes into account six major parameters namely yield, cost of raw materials, safety, infrastructure, time, and purification. (Aken et al., 2006) Penalty points are given for each of these six parameters if they are compromised and these penalties are deducted from a total of 100. This means higher values on this eco scale are considered to be greener and better processes. Table 1 shows data for the 3 processes described above suggesting that the Hoechst Celanese process is the greenest route of the three. Companies in India must try and use this method of synthesis for obtaining overall best results since most companies still synthesize paracetamol through the conventional process of hydrogenation and then acylation.

Continuous Process of Manufacture of Paracetamol

Any manufacturing process based on feeding and removing materials without any stoppage in the synthesis is called a continuous process. The advantages of a continuous process include easier scale-up, reduced costs, and greater social impact by decreasing environmental problems. (*Download.Pdf*, n.d.) Additionally, continuous flow processes typically profit from stable product quality once steady state conditions have been achieved, thus decreasing required quality control measures and avoiding changes in product quality as observed in typical batch chemistry. Figure 6 shows a flow diagram of a continuous process for the synthesis of paracetamol. A lot of Indian companies still use the conventional batch process to manufacture paracetamol. However, the national chemical laboratory (NCL) under the council of scientific and industrial research (CSIR) has developed a technology which is efficient and greener for paracetamol syntheses. This technology can benefit Indian manufactures to be less dependent on cheaper Chinese counterparts who are leaders in global production of paracetamol. From table 1 we can see that acetic anhydride adds a significant cost in the manufacturing process of paracetamol. However, the NCL process does not use acetic anhydride in its process, and due to this the production cost is reduced by 15-20%. Conventional batch processes generate lots of aqueous effluents, have a high footprint, and give inconsistent quality of product. However, the CSIR-NCL has developed a continuous mini-pilot scale plant which requires less space. (*NCL Develops Superior, Cheaper Technology for Paracetamol; 2 Firms Sign NDA*, 2019)

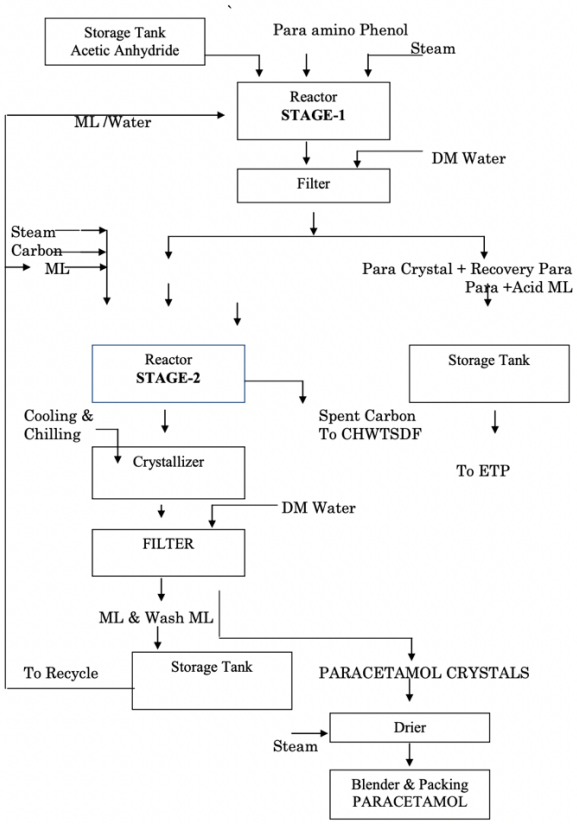

FIGURE 6. Continuous manufacturing process of paracetamol *(*0_0_25_Feb_2016_1108554031AnnexureManufacturing&EffluentTreatmentProcess.Pdf*, n.d.)*

Conclusion

From this paper's initial analysis of the Indian pharmaceutical industry, there is huge potential for the industry to grow quantitatively and qualitatively if there is increased research in the pharmaceutical field, and consistently relatively low prices of produced drugs produced. Most importantly, the application of AI and ML tools as these technologies are growing at an exponential rate, and all organizations are racing towards faster growth and revenue generation. Shipping routes, predictive power, navigation technologies, and quality control are a few of the several applications of AI and ML tools summarized in the paper. At the same time companies must also constantly improvise their traditional methods of synthesis of pharmaceuticals which both increase their efficiency as well as make them greener routes of synthesis.

Overall, organizations globally are showing significant improvements in forecasting error rates, price lowering, and on-time shipping of material using AI and ML tools. The major Indian pharma companies must rebuild cautiously with certain modifications like managing inventory, being more self-sufficient, and having efficient logistics that can boost the growth of this industry in India. India's appeal in the pharma industry is growing in various aspects. It has always been a formidable player in the pharmaceutical industry but with its increasing socio-economic relations with different countries in

the world and increasing scientific expertise and economy, India can further enhance its presence in the pharmaceutical industry worldwide. COVID19 prompted companies to realize to not be heavily dependent on any country for a source of raw materials, particularly India on China. The COVID19 pandemic has alerted the world and demonstrated the necessity that supply chain management must be approached in a more systematic and combined manner to build a stronger national network. A well-known Charles Darwin quote is ideal for the situation – "It is not the strongest of the species who survive nor the most intelligent that survives. It is the one that is most adaptable to change."

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