International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1939-1945 www.ijprajournal.com ISSN: 2249-7781

Recent Automation of Industry 4.0 In Pharmaceutical Manufacturing

Apeksha Mule[1], Aboli Puranik[2], Prof. K. N. Tarkase[3]
[1,2,]*Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy, Ahmednagar, Maharashtra, India-414111*
[3]*Assistant Professor, Department of Pharmaceutical Quality Assurance, Dr.V.V.P.F's college of Pharmacy, Ahmednagar-414111.*
Corresponding Author: Apeksha Mule[1]

Submitted: 15-05-2023 Accepted: 30-05-2023

ABSTRACT: Over the last centuries, medicines have evolved from crude herbal and botanical preparations into more complex manufacturing of sophisticated drug product and dosage form. This review focuses on the implementation of automated technologies in pharmaceutical industries and pharma industry evaluation towards the industry 4.0(Artificial Intelligence). Automation is used to improve safety and reduced human errors. Future smart factories will incorporate autonomous features that will increase production flexibility and agility.

KEYWORDS: (11 Bold) Actuator, Microprocessor, Enginehead, L293D Current Amplifier, IRF 3205 MOSFET.

I. INTRODUCTION

1.1Industry 1.0

Automation is the use of advanced machinery and technology to boost the output of pharmaceutical research and manufacturing, with robots playing a key role in this process. The traditional batch techniques and earlier business models are being challenged by Industry 4.0, which is advancing pharmaceutical production technologies. [1] During the COVID-19 pandemic, manufacturing techniques that are flexible, more sensitive to changing demand, and less dependent on human intervention throughout production are crucial. New ways of thinking will be required to apply Industry 4.0 for medicines and overcome the inertia of the current industrial infrastructure, operations, and regulation. [2] Automation increases productivity yield while having less negative consequences on cross contamination, product exposure, and yield. [3]

If Industry 4.0 is the present, then Industry 1.0 is the starting point of the current pharmaceutical sector. Throughout the course of civilization, herbal or botanical compounds have been used as remedies. Industry 1.0 witnessed the move from basic hand-operated instruments to industrial scale machinery capable of crushing, milling, blending, and pressing bigger amounts of medicines during the manual processing of botanical, mineral, and animal derived materials.[1]

1.2 Industry 2.0

Electricity as well as early electronic machines and assembly lines with pre-set controls that incorporated basic automation and process controls that provided manufacturers with the ability to set basic process parameters enabled the second industrial revolution. This manifested as electronic machine-based crushing, milling, blending, and tablet pressing in the pharmaceutical manufacturing industry, allowing for larger-scale production and, more importantly, more monitoring of processes and quality.

1.3 Industry 3.0

The creation and accessibility of computer and communication technologies, including networked computing, the internet, and wireless communications, contributed to the third industrial revolution. These technologies allow for greater automation of machinery and processes, which in the pharmaceutical industryenabled ideas like continuous manufacturing and active control.

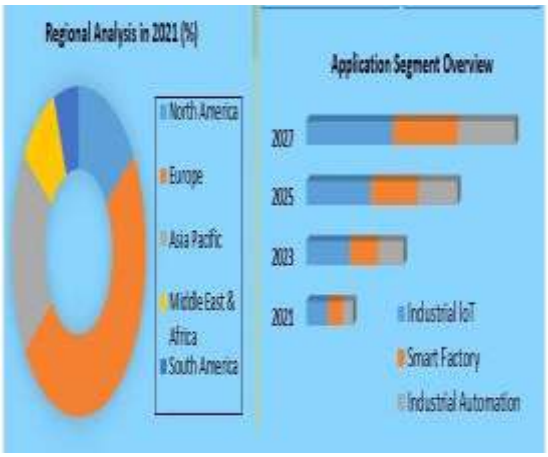
Remote sensing and monitoring also allowed for better tracking of production-related metrics and parameters while reducing the need for human operators on the factory floor. While some industries have now fully embraced Industry 3.0, the pharmaceutical sector is still very much in the early stages of this change. For instance, continuous manufacturing, a technology that has been widely implemented in other industries, involves sending materials created during each process stage immediately and constantly to the following phase for additional processing. [1]

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1939-1945 www.ijprajournal.com ISSN: 2249-7781

1.4 Industry 4.0

The integration of cutting-edge manufacturing technology during the fourth industrial revolution opens the way for integrated, autonomous, and self-organizing manufacturing systems that run without the need for human intervention. Manufacturing of pharmaceuticals has undergone a widespread transition into Industry due to the experience gained in the automated and digital environment of Industry 3.0. The journey from basic data collection to digital maturity involves the transformation of data from raw manufacturing process data captured to information gained through analysis to knowledge formed through the addition of contextual meaning, possibly by artificial intelligence, and finally to actionable wisdom to guide decision-making by the contribution of insight.

Autonomous systems and cyber-physical machines, which have mechanisms controlled by computer algorithms and are capable of self-optimization, judgement and decision-making, remote movement, and adaptive control, are propelled by this "wisdom." [1,3]



II. INDUSTRY 4.0 TECHNIQUES UTILIZED IN PHARMACEUTICAL MANUFACTURING

Industry 4,0 environment is the integration of connectivity, artificial intelligence (AI)and robotics to enable system that operates with employees or workers.

Integrated autonomous and robotic system fuse actual time and online data with industrial production processes and artificial intelligences in order to optimize manufacturing and co-operate wide management.

During these phases, data undergoes transformation from unprocessed signals obtained

Advantages:

- Increase efficiency and output: Automation may enhance efficiency and output by lowering human error rates, improving speed and accuracy, and handling tasks that are challenging for humans to complete.
- Reduced cost: Support automation can lower costs by saving on personnel, energy, and material costs.
- Improved safety: Automation can reduce the risk of human errors and perform tasks that are too dangerous for humans.[4]

Disadvantages:

- Dependency on technology: Automation also creates reliance on technology. If something goes wrong with the machine or the software, it can cause significant disruption.
- Income inequality: A general fear is that automation will lead to income inequality as machines replace jobs. [4] from a system to fully developed digital maturity. Data are originally gathered throughout the manufacturing process, structured through data digitalization and analysis as Big Data, then synthesised into knowledge by the meaning deduced via artificial intelligence, and ultimately reached through the combined insights of digital maturity.

[1]

2.1. Digitization and digital maturity

The digitization of multiple complex pieces of the pharmaceutical value chain with embedded cybersecurity is a key to implementing industry 4.0. A critical concept in developing the so-called “smart factory” is the industrial internet of things (IoT), which is a type of cyber-physical system comprising interconnected computing devices, sensors, instruments, and equipment integrated online into acohesive network.

The IoT needs data digitization, which is the transformation of already manually captured data to digital device captured data. In pharmaceutical manufacturing this might provide chain-related information like raw materials variability and global tracking of materials across facilities.

While the distinct tools developed to optimize key value drivers may vary depending on the core competencies and business models of pharmaceutical firms, the development of more

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1939-1945 www.ijprajournal.com ISSN: 2249-7781

integrated systems will be consistent. It is the digital integration into an IoT that could produce divisive pharmaceutical applications following as real-time, on-demand, small-scale production systems, truly customized dosage forms, and revolutionary biosensor diagnostics. [1,6]

2.2 Artificial intelligence

Tasks that depend on computer-based intelligence may involve reasoning, critical thinking, learning, and decision-making among others. AI includes a spectrum of sub-disciplines that take varied approaches to designing computer intelligence depending on the applicable features and tasks to be performed, such approaches involve handling wide and disparate datasets with specific algorithms.

Within the province of AI, and owing to the advancements in available technology and software programming, machine learning (ML) and artificial neural networks (ANN) have emerged as two of the alternative advanced strategy for prediction and risk management. [6]

2.3 Full Automation

Complete strategy automation entails the collection of all process performance data using cloud-connected PAT technology, processing of that data into organised information, and application of AI-based algorithms to that information in order to gain insight into and improve process control.

By putting those concepts into practise, it may be possible to alter the real-time recording of process performance parameters and trends, which may then be used to predict product quality attributes later on in the process. [1]

III. THE CHALLENGES TO IMPLEMENTING INDUSTRY 4.0 IN PHARMACEUTICAL MANUFACTURING

Obstacles to implementing industry 4.0 in the production of pharmaceuticals. Adopting cutting-edge manufacturing technology, overcoming technical, logistical, and regulatory obstacles are necessary for achieving Industry 4.0. A more autonomous manufacturing environment with improved process controls and more developed quality management should result from each step taken on the approach to an Industry 4.0 manufacturing environment.

With these modifications, there should be less variation between lots and a more reliable supply of products. While many pharmaceutical producers are comfortable with the fundamental tools of PAT and QbD, fewer are prepared to take the next steps and implement cutting-edge technologies in support of smart production. The extensive institutional and regulatory knowledge amassed on existing platform technologies is a fundamental factor in the delay in adopting newer technology.

Many industries are interested in adopting a "first to be second" strategy by observing how competitors adopt new manufacturing technologies and how regulators react due to the absence of precedent in the industry, the costs associated with development, and the potential regulatory issues.

3.1 Regulatory barriers

Regarding regulatory barriers, functioning within the current regulatory frameworks may be regarded as a real or tangible difficulty for technical innovation. Lack of regulatory precedence may cause the industry to stick with outdated practises even when new ones can ultimately result in less regulation overall and higher quality. Even currently used Industry 3.0 technologies, such those for continuous manufacturing and adaptive control systems for product release, have challenged the prevailing paradigms for process validation from the previous 50 years to the challenge. The burden of submitting regulatory applications across multiple international jurisdictions with diverse regulatory expectations, particularly for new industrial technology, is another regulatory barrier. Global regulatory convergence on new manufacturing technology may help manufacturers become less apprehensive.[1]

Over the past ten years, the American Food and Drug Administration (FDA) has pushed for further performance-based regulation. Performance-based regulation & Industry 4.0 go hand in hand and can even be mutually enabling. Performance-based regulatory systems concentrate on a predetermined specific outcome so that regulatory actions can then concentrate on identifying performance measures that ensure an adequate safety margin and providing incentives to improve safety without formal regulatory intervention. The extensive data and analysis made possible by Industry 4.0 will allow the industry and regulators to identify the fundamental set of critical control points which can fully ensure that the critical quality criteria are met. As a result, the production system can continually evolve and

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1939-1945 www.ijprajournal.com ISSN: 2249-7781

gradually improving by consistently optimizing various parameters while consistently creating high-quality products.

Monitoring risks related to these parameters constant modification with little to no effective regulatory oversight will be a major challenge for regulators. The pharmaceutical industry is still very much uplifting into Industry 3.0 by adopting continuous manufacturing and implementing advanced PAT. In an Industry 4.0 environment, performance-based regulation may need to be recognised by bringing together advanced manufacturing technologies and advanced regulatory systems to enable real-time assurance of production system performance. Consequently, some producers continue to adhere to the Industry 2.0 model. Regulating asector where some pharmaceutical companies continue to operate under Industry 2.0 standards while others migrate to Industry 4.0 at varying rates is a significant challenge. This will create a situation where the regulated industry includes Industry 2.0, 3.0, and 4.0 at the same time. In order to enable the adoption of novel technologies without adversely impacting the supply of products still made with older technologies, regulatory frameworks that are flexible or amenable to all technology paradigms will be required to accommodate the coexistence of old and new technology paradigms (possibly even within the same company). [1]

3.2 Technical challenges

The technical challenges that Industry 4.0 implementation will experience will be those that are discovered and overcome by early adopters. The current manufacturing paradigm seems to have some technical limitations, including rigid process parameters, the use of extensive offline testing (especially for sterile products) &the frequent involvement of humans in manufacturing operations, although some manufacturers may not be willing to accept these challenges. For contrast, analytical technology may not be sufficient to allow the real-time release of pharmaceutical products. However, end-to-end automation and client demand-driven production, operations, and even dispensing may be facilitated by enhanced PAT combined with a cloud-based infrastructure and advanced processing capacity to apply artificial intelligence.

The majority of industries are now figuring out how to manage the "Big Data" era, which requires acquiring, processing, and retrieving vast volumes of both stored and real-time data. Industry 4.0 demands an enhanced data and computing infrastructure that blends software and hardware to rapidly supply the information required about a process or product for manufacturers to evaluate the efficacy of their processes. Making judgments about how to use knowledge and insights generated from big data, which could be used for internal auditing, product release decisions, marketing, and/or sharing with regulatory authorities, is one of the challenges of the technology. Big Data provides the foundation for all IoT interactions, communications, and mutuallearning. One major technological challenge in this project will be determining and conveying the data's purpose.

New techniques of automated communication between networked machines and devices are being developed as a part of the ongoing development of wireless communications protocols. These techniques will significantly reduce or eliminate the need for human intervention in a variety of tasks, minimising the risk of human error. For instance, to assemble the integration and digitization of a smart facility, analytical testing, equipmentmaintenance, adaptive process control systems, and quality control testing will need to be compatible across software and hardware elements & rely on communications across networked devices. Companies will need to adopt risk mitigation strategies in an Industry 4.0 setting to mitigate or eliminate network vulnerabilities. In order to prevent operations involving networked devices and manufacturing equipment from being interrupted or threatened in the future, data and system architectures will need to be strengthened. [1]

3.3 Logistical challenges

The implementation of Industry 4.0 will encounter logistical challenges, and in some circumstances, industry and regulators may compete for the same limited resources. Manufacturers and regulators will be expected to make cultural shifts & innovations in order to tackle various data, computing, automation hazards on the way to full adoption of Industry 4.0 approaches. In order to adopt a new paradigm and industry infrastructure based on digitalized and interconnected enterprise systems that rely on computational power, communications technologies, cybersecurity, and advanced controls in order to achieve optimization, knowledge and training gaps will need to be loaded. Robust training programmes will be essential because there

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1939-1945 www.ijprajournal.com ISSN: 2249-7781

will eventually be new labour force training requirements.

The use of AI-based mathematical models is a core componentof Industry 4.0. The collection of historical data from innovative production techniques including continuous manufacturing is the first step in turning the concept of AI control become reality. If businesses use cooperative, non-competitive, or open innovation strategies to access these historical process data, machine learning might well be simplified. This is a paradigm shift from the prevalent "closed" strategic model, in which each corporation stores all of its data and information internally. Intellectual property and intellectual property rights are a restriction that could need to be addressed in this context.

In the conclusion, it could be necessary for manufacturers and regulators to work together effectively and communicate frequently in order to fully utilize the advantages of Industry 4.0.

IV. CONCLUSION

Through developments in digitalization, autonomous systems, robotics, and computers, Industry 4.0 technologies have the potential to alter pharmaceutical manufacturing and logistics platforms. Particularly, there may be considerable advancements in the frameworks for the pharmaceutical supply chain, production procedures, distribution, and stock. Future smart factories will incorporate autonomous features that will increase production flexibility and agility. Advancements and innovations must be made to overcome several data, computing, and automation risks and challenges if Industry 4.0 is to be fully adopted. Industry and authorities are acquiring skills in modelling and simulation, sensor systems, data management, data analytics, computational and control engineering methodologies required to support autonomous systems, artificial intelligence, and computer infrastructures in so that they are ready for smart manufacturing systems.

It could be necessary to reconsider enterprise-level systems like quality management and training.[3] We are starting to recognise issues with current approaches to regulatory compliance and start to

uncover known or unknown risks related to these novel techniques. Eventually, we aim to establish regulatory frameworks that support Industry 4.0.

The evaluation of digital implementation tries to pinpoint any possible risks, advantages, and difficulties brought on by digitization. The pharmaceutical sector can address problems due to digital implementation assessment. [5]

Future prospective

Because the majority of rules were created in an Industry 2.0 paradigm of batch manufacturing, the adoption of the advanced manufacturing technologies of Industry 4.0 may present difficulties for the current regulatory framework. Demand may change in the future as a result of the generation of more, more readily available, and real-time information about product quality that may be more transparent to purchasers, payers, healthcare providers, and patients. Such transparency would encourage additional investment in tools that can reliably produce high-quality products.

The ultimate beneficiaries of Industry 4.0 in pharmaceutical manufacturing, however, shouldn't be drug producers or regulators; rather, it should be the patients who will get access to better-quality drugs with more dependable supply chains that are less likely to experience shortages.

Abbreviation

AI- Artificial intelligences
IOT- Internet of things
ML- Machine learning
ANN- Artificial neural network
PAT-Process analytical technology
QbD- Quality by Design

REFERENCES

[1]. N.Sarah Arden, Adam C.Fisher, Katherine Tyner, Lawrence X.Yu, Sau L.Lee, Michael Kopcha, Industry 4.0 for pharmaceutical manufacturing : Preparing for the smart factories of the future, International Journal of pharmaceutics, 2022, 602:120554.

[2]. D,Ntama, E.Lopez-mantera, J.Mack,C.Omar, M.I.Higet, D.Mass, N.mitchell, P.Soulatinark, P.Z.Moghadam, M.Zandi, Industry 4.0 in Action: Digitalisation of a Continuous Process Mfg. for formulated products, Digital Chemical Engineering, 2022,3:100025.

[3]. Thomas George, Palamaltathkuttiyil, Hemanth Kumar Somareddy, Shailesh Thirumaleshwar, Mysore Prakash Gowrav, Impact of Automation in Pharmaceutical Industry on Roles and

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 1939-1945 www.ijprajournal.com ISSN: 2249-7781

Responsibilities of quality Assurance, 2020;11(1):166-172.

[4]. Team capacity, What is the best way to describeautomation?, Capacity, Jun 27 2022, https://capacity.com/supportautomation/faqs/what-is-the- best-way-to-describe-automation/

[5]. N. Nurlaela Arief, Aurik Gustomo, M. Rahman Roestan, Aghania Nadhira Aliya Putri, Muthya Islamity, Pharma 4.0: anaylsis on core competence and digital levelling implementation in Pharmaceutical industry in Indonesia, Heliyon, 2022, 8: e1037.

[6]. Gioia Volkmar, Peter M.fischer, Sven Reinecke, Artificial Intelligence and Machine Learning : Exploring drivers, barriers and future developments in marketing management, Journal of Business Research, 2022,149:599-614.

[7]. Industry 4.0 Market: Global Industry, Analysis and Forecast(2022-2027) by Technology Type, End user industry and region, Information technology and telecommunication,viewed March 2022.

[8]. https://www.maximizemarketresearch.com/market- report/global-industry-4-0-market/35222/

[9]. Yingjie Chen, Ou Yang, Chaitanya Sampat, Pooja Bhalode, Rohit Ramachandran, Marianthi Ierapetreious, Digital Twins in Pharmaceutical and Biopharmceutical Yingjie Chen, Ou Yang, Chaitanya Sampat, Pooja Bhalode, Rohit Ramachandran, Marianthi Ierapetreious, Digital Twins in Pharmaceutical and Biopharmceutical

[10]. Arinez, J., Chang, Q., Gao, R., Xu, C., Zhang, J., Artificial Intelligence in Advanced Manufacturing: Current Status and Future Outlook. J. Manuf. Sci. Eng. 2020,142 (11):16.

[11]. Atobe, T., Mori, M., Yamashita, F., Hashida, M., Kouzuki, H., Artificial neural network analysis for predicting human percutaneous absorption taking account of vehicle properties. J. Toxicology. Sci. 2015,40 (2), 277–294.

[12]. Balasegaram, M., Kolb, P., McKew, J., et al., An opensourcepharma roadmap. PLoS Med. 2017 14 (4):e1002276.

[13]. Fakhreddin F. Rad, Pejvak Oghazi, Maximilian Palmié C. Patel, Setayesh Sattari, Industry 4.0 and supply chain performance: A Systematic literature review of the benefits, challenges and critical success factors of 11 core technologies, Industrial Marketing Management, 2022, 105:268-293.

[14]. Baoyang Ding, Pharma Industry 4.0:Literature review and research opportunities in sustainable pharmaceutical supply chains, Environmental Protection, 2018, 119:115-130

[15]. Banks, L., 10 Disruptive Technologies that will Transform Pharma. Pharmaphorum,2015.

[16]. Baur, C., Wee, D., 2015. Manufacturing's Next Act. McKinsey

[17]. Berry, I.R., Nash, R.A., 2003. Pharmaceutical process validation. In: Nash, Robert A., Wachter, Alfred H. (Eds.).

[18]. Biophorum/BPOG,2017.Automated Facility https://www.biophorum.com/wp-content/ uploads/2017/07/Automated-Facility.pdf. Accessed.

[19]. Buvailo, A.,The Why, How and When of AI in thePharmaceutical Industry, 2018.

[20]. Ekins, S., 2016. The Next Era: Deep Learning in Pharmaceutical Research. Pharm. Res. 33 (11):2594–2603.

[21]. Grossman, J.,The Four Stages of Digital Maturity: How Does Your Organization Rank? Forbes. l, S.A., 2016, Policymaker's Guide to Smart Manufacturing. InformationTechnology & Innovation Foundation, 2018.

[22]. Peter Guilfoyle,Northwest Analytics,Pharma 4.0: Industry 4.0 Applied to Pharmaceutical Manufacturing. Pharmaceutical Process World, Oct. 2018.

[23]. Jovanis, M. Digitizing to Modernize Manufacturing. Pharmaceutical Technology, 2019, 43 (4):63–65.

[24]. Louis Allen, Jack Atkinson, Dinusht Jayasundara, Joan Cordiner and Peyman Z.Moghadam, Data visualization for Industry 4.0: A stepping-stone toward a digital future, bridging the gap between academia and industry, Pattern, 2021, 2.

[25]. Prince Chacko Johnson, Christofer laurel, Mart Ots, Christian Sandstrom; Digital innovation and the effects of artificial intelligence on firms research and

development Automation or augmentation, exploration or expoitaton ?, Technological Forecasting and Social change 2022, 179:121636.

[26]. Gioia Volkmar, Peter M.fischer, Sven Reinecke, Artificial Intelligence and Machine Learning : Exploring drivers, barriers and future developments in marketing management, Journal of Business Research, 2022, 149: 599-614.

[27]. Janja Zagra , Jurij Mihelic, Big data Collection in Pharmaceutical Mfg. and its use for product quality predictions, Scientific data 2022,9:99.

[28]. Heriberto Garcia Reyes, Jonnaton Avilise-Gonzalez, Sania Aviles-Sacoto, A Model to Become a supply chain 4.0 Based on a digital maturity perspective, procedia computer science,2022, 1058-1067.