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A Review: Evaluation & Modernization of Pharmaceutical Industry (4.0)"

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Overview

Industry 4.0 is a new industrial revolution that uses cyber-physical technology to improve system intelligence. The use of autonomous devices and systems is crucial in the manufacture of pharmaceuticals and has the potential to bring products to market with high levels of quality, low cost and time. The R & D phase of developing a new drug or drug can be very long and costly compared to traditional products, so applying Industry 4.0-related technology to the drug development process could bring significant benefits to the biomedicine and pharmaceutical industry. there is. It also could open new windows for regulators to track and track all stages of the drug development process with less effort. This chapter describes the first various phases of the drug development process, then details the use of computers and digital technologies in each phase, and finally introduces the Pharma 4.0 ecosystem.

Industry 4.0 is the latest move towards intelligent automation technology. In this new era, the integration of modern manufacturing and new information technologies will play an important role in economic competitiveness . This review examines future technological trends in the pharmaceutical industry. In the pharmaceutical industry, Industry 4.0 can support extended manufacturing personalized medicine, layered modeling, localized 3D printing of treatments, and even a future in which humans are no longer closely involved in production. This future will be possible when industry and educational institutions work together to promote advanced research and implementation of Industry 4.0. With the advent of the new cyber-physical system design paradigm, the variety of systems that future enterprises will need to collaborate with has increased significantly. Industry 4.0 is an industrial approach that addresses all aspects of the industrial management model, including culture, management accountability, and regulatory interaction. Manufacturing is moving from mass production to mass customization , with industry 4.0-related trends such as data integrity by design, overall control strategy, personalized processing, and industry-wide end-to-end supply chain integration. Is spurring on. Industry 4.0 will enable cyber and physical systems to work together to build smart factories by redefining the role of humans in manufacturing. Industry 4.0's new technology enables the creation of sustainable value, leading to a more agile and intelligent personalized pharmaceutical industry, enabling pharmaceutical companies to achieve a competitive advantage. A more sustainable drug supply chain needs to be implemented to coordinate future operations and management throughout the drug lifecycle. The 4.0 technology emerging industry is now aiming for flexible and localized production close to its customers. Manufacture "on demand" and try to avoid large inventories. Innovative, adaptable technology helps pharmaceutical companies establish a more robust and agile manufacturing process that features reduced interruptions, reduced errors, and improved quality control .

Keywords: Industry 4.0 · Pharma 4.0 · Intelligent manufacturing · Drug development process

Introduction

Three major revolutions in the manufacturing industries have already occurred: Industry 1.0 was introduced when mechanization and steam power were employed to perform over human power processes, Industry 2.0 was introduced when mass production and electric energy provided a huge improvement in the productibility level of manufacturing systems, and Industry 3.0 introduced the power of automation, computer, and IT to the manufacturing industries. The fourth industrial revolution has been called Industry 4.0 .Consider a production system with robots, CNC machines, automatic storage, and handling systems and operators that communicate with one another using a computerized network system, and each of them autonomously rearranges their operation through a cloud-based central decision-maker. Imagine a city where transportation systems, traffic control systems, grid, ports, healthcare systems, parking, waste management systems, and air pollution control systems negotiate with each other, and a cloud-based intelligence system arranges all operations on an optimal level to promote safety and cost issues of the people. Imagine a health center that can communicate with many different sections, aiming to provide the finest quality of services. These are a few examples of the future of Industry 4.0 that could be enabled by cyber-physical systems (CPS) technology.. CPS is defined as the calculation, interconnection, and integration of physical processes for the purpose of controlling the process. CPS is a combination of nodes with different roles and properties. These nodes adapt to new states based on the knowledge available in the system and the actual feedback from other nodes.

This technology, which is changing the way people interact with industrial systems, is very similar to the Internet, which has changed the way people interact with IT and information. Industry 4.0 uses CPS technology to bring intelligence to the system. CPS consists of many different and heterogeneous elements that require research to properly define each subelement and its specifications. The main technologies are the Internet of **Things (IoT)**, **artificial intelligence (AI)**, **cloud computing (CC)**, smart embedded devices, and the Internet . These technologies are at the core of CPS, but several other technologies such as digital twins, cloud manufacturing, virtualization, and green waste management can play a supporting role.

The role of CPS in pharmaceutical manufacturing has the potential to transform the control and management systems of biotechnology and pharmaceutical companies into what can be called the Pharma 4.0 revolution. These changes include reliable medical devices and systems, drug design and development, on-demand drug manufacturing, 3D printed drugs, Logistics 4.0 for drug distribution management, and green waste management. In pharmaceutical production where timing accuracy and quality issues are not noticeable, it is easy to consider and adopt new models such as "collaborative network organization" and "collaborative design & development". Autonomous and connected facilities can significantly increase the productivity of the pharmaceutical industry, leading to more effective detection and recovery of defective products.

Cyber-Physical Embedded PAT can significantly improve system intelligence and product quality and reduce reliance on human decision making. In monitoring, regulatory oversight benefits from a distributed consensus on the available bandwidth and technology of distributed control technology. Consumer networks can change dramatically at the right time. A distributed real-time quality controller that integrates sensors and actuators can change the nature of the Internetquelle1 **real-time release test (RTRT)** system. The economic impact of any of these applications is enormous. However, today's pharmaceutical industry can unnecessarily impede progress towards these applications. This chapter first briefly discusses Industry 4.0 technology, then the computing applications of the pharmaceutical and biotechnology industries, and finally the Pharma 4.0 ecosystem, and several (potential) exit applications.

Emerging 4.0 Technologies.

The industry today aims for flexible and localized production close to its customers. Manufacture "on demand" and try to avoid large inventories.

Adaptive and innovative technology helps pharmaceutical companies establish a more robust and agile manufacturing process featuring reduced interruptions, reduced errors and improved quality control . .. Vertical integration of Industry 4.0 will upgrade pharmaceutical manufacturing plants to "reconfigurable factories", allowing flexible, agile and intelligent production lines to support mass customization of personalized medicines to meet different needs. Will be . Efficient cross-company communication and big data analytics can improve process monitoring performance and detect and reduce material waste, overproduction, and energy consumption .

Topics covered in this article include Augmented Reality (AR) and Virtual Reality (VR). 3D printing and personalized medicine; digital twins and simulations. Cyber physical system, cloud.

Industry 4.0

Industry 4.0 is a new chapter in the Industrial Revolution related to the use of cyber-physical system technology in manufacturing, aimed at increasing system intelligence through networking, automation, machine learning and real-time monitoring. Figure 1 shows a schematic diagram of the CPS. As shown in the figure, the system contains several physical objects such as CNC machines, robots, automations, etc.0 Designer mobile and data capabilities. Imagine a computer. This entire physical object is an embedded device connected to the Internet. In addition, these devices include processors for decision making. Devices on the network are to exchange data with cloud services for monitoring and control using IoT technology and the Internet. To identify devices on the network, IoT technology provides nodes in the network with unique identities. The status of the device is captured by the sensor and monitored by the cloud service. The device is controlled by a cloud service using comments generated by AI tools and shared with the device via the IoT. The main goal of using CPS is to improve the intelligence of resources (devices, humans, etc.) and the level of integration between resources.

Drug Development Life Cycle:

Drug development is a step-by-step process that involves a series of stages, including drug discovery, preclinical trials, clinical trials, approval processes, and post-marketing surveillance. The following subsections briefly describe each of these steps.

Drug discovery: which is the first step of drug development process, brings thousands of potential candidate compounds as a medical treatment. However, only a few numbers of compounds have been forwarded to the next steps after early testing. Commonly, drug design and discovery are performed through the following steps:

Focusing on a disease process and etiologies to discover and identify a proper target

- Finding or designing a compound that interacts with the specified target to change disease situations
- Finding possible beneficial effects for lead identification by performing numerous molecular compound tests
- Searching among the unforeseen effects of current treatment protocols, aiming to find a possible new effect on the target
- Synthesizing a novel compound from existing materials that will be effective in manipulating the target

Ecosystem Pharma 4.0:

Ecosystem pharma 4.0 is a manifestation of Industry 4.0 in the pharmaceutical industry and can be defined as employing the medical cyber-physical system (MCPS) in any stage of the drug development life cycle (Ding 2018). MCPS refers to life-critical,context-aware, networked systems of medical tools and devices that are collectively involved in the treatment protocols of a patient. The main missions of using this paradigm in the drug development process are to reduce the developmental costs and cycle time and also to improve the quality of the drug products by(a) improving the smartness of the contributors (i.e., humans, tools, and devices),(b) connecting and integrating the smart contributors, and (c) providing real-time status and awareness information to the stakeholders and the regulatory authorities. MCPSs employ the technology of cyber-physical systems (CPSs) to provide high-quality continuous care for patients in complex medical scenarios such as clinical trials. CPSs are integrations of computation, networking, and physical processes. Embedded computers and networks monitor and control the physical processes with feedback loops, where physical processes affect computations and vice versa. Figure 1demonstrates the Pharma 4.0 ecosystem. It shows the process of collecting big data from several sources into a data pool and then performing the necessary analytics using AI, ML, or cognitive process to predict stream line drug life cycle processes. The ecosystem connects two separate worlds of embedded tools and devices (ETDs) and cybernetics in the life cycle of medicines. As shown in the figure, the drug life cycle includes three major steps: joint drug development, intelligent drug manufacturing, and post-marketing recognition systems. Other stakeholders, including regulatory agencies and customers, are also connected to the system via cybernetics. Cybernetics uses a variety of AI techniques and tools for decision making, communication, and automated control of healthcare systems. The ecosystem supports the Green Drug Lifecycle System. medical systems use less natural resources, reduce pollution and waste, recycle and reuse materials, and reduce emissions in the process. On the way to Pharma 4.0, we outlined current data science applications in various phases of the bioprocess life cycle. Recently, a Pharma 4.0 application in smart drug manufacturing was reported, and the author proposed a cyber physical-based PAT (CPbPAT) framework for implementing smart manufacturing systems in the pharmaceutical industry .The impact of data analysis techniques, digitization, Industry 4.0, artificial intelligence, digital twins, and continuous manufacturing on Pharma 4.0 has recently been reported in another paper.

The Need for Artificial Intelligence in Pharma 4.0:

Artificial intelligence in medicine and healthcare is growing rapidly. It uses a variety of software and complex algorithms to simulate human intelligence and cognition to analyze and interpret comprehensive complex healthcare and Medical data. AI has used different computational approaches and techniques in different medical disciplines, especially in diagnostic and therapeutic protocols

Medical AI has been able to recognize significant correlations in the data provided in many clinical conditions to help diagnose, treat, or predict non-clinical conditions such as medical conditions and laboratory tests. In medicine, this technology is rapidly evolving as a reliable solution to complex situations. With the development of new smart devices, such as wearables, smartphones, and biosensors, some techniques of AI, like deep learning, can deal with the provided big data of such smart devices meaningfully AI in pharmaceutical sciences and drug development process is associated with the use of different automated approaches and techniques to replace the traditional methods that rely on the human brain with these new technologies. It is not surprising that almost all aspects of the pharmaceutical industry, from drug discovery and laboratory studies to clinical researches of drug development, epidemic predictions, remote monitoring, and regulatory supervision, manufacturing processes, and marketing, can apply AI, which leads to increased operational efficiency and cost-effectiveness. AI can help to design and identify new molecules based on target validation very effectively. Complicated pharmaceutical and pharmacological networks with large databases always need to solve different complex issues and challenges, and AI is one of the best approaches to identify obscurant patterns between diseases, drug composition, and developmental qualities. Machine learning is currently merging quickly evolving methods in computer-aided drug discovery. To develop drugs with significant biological and chemical properties, ML is an applicable tool that mines chemical and biological information from large databases. To predict the physical, biological, and chemical properties of new compounds, the ML method uses pattern recognition algorithms to empirically differ significantly from physical models that rely on physical equations such as quantum chemistry. Build a generalized mathematical model under the results. Converting a composite structure into the chemical information used in the ML technique requires multi-layered computation (that is, chemical graph acquisition, descriptor generation, fingerprinting, similarity analysis). Each layer has a significant impact on the quality of the chemical data and is built on the previous layer. Machine learning methods can be divided into supervised learning and unsupervised learning. Supervised machine learning models include regression analysis, k-nearest neighbors (kNN), Basilian probability learning, SVMs, random forests, and neural networks. Unsupervised techniques include dimensionality reduction techniques such as: B. Principal Component Analysis (PCA), Independent Component Analysis (ICA), and several supervised methods that can support unsupervised learning (eg B. SVM, probabilistic graphical models and neural networks. Another of the unsupervised algorithms. One family is clustering algorithms. Discovering abuse relationships between chemical structures and their SAR or biological activity is one of the major areas of application of ML in drug discovery. Achine learning techniques can be used to model QSARs or quantitative structure-activity relationships (QSPRs) to develop artificial intelligence programs that accurately predict in silico how chemical modifications affect biological behavior. Many physicochemical properties of drugs, such as toxicity, metabolism, drug-drug interactions, and carcinogenesis, are effectively modeled by quantitative structure-activity relationship (QSAR) techniques. QSAR is a very important strategy in chemistry and pharmacies, based on the idea that changing the structure of a molecule changes the activity and properties of a substance . The general protocol for building QSAR models for drug discovery is systematic and consists of several modular steps, including chemo informatics and machine learning techniques. The first step is "molecular coding". This coding searches for experimental results to see if chemical features and properties are derived from the chemical structure. It then uses unsupervised learning techniques to perform feature selection steps to identify the most relevant features and reduce the dimensions of the feature vector. Finally, in the learning phase, a supervised machine learning model is applied to detect empirical functions (explicit or implicit) that can achieve the optimal association between the input feature vector and the biological response (Hunter). Computational drug discovery provides researchers with pharmacodynamic and pharmacodynamic information such as absorption, distribution, metabolism, excretion, mechanism of action, route of administration, side effects and toxicity, demographic changes, and drug-drug interactions. Helps identify promising compounds for development to improve. In the pharmaceutical R & D process, the combination of cloud

computing power and AI makes the process faster, more cost-effective, and more accurate. These benefits allow large companies to evaluate different new approaches to developing traditional drugs in the old and new categories at the cellular and molecular levels using AI with the high computing power of the cloud. It becomes more important when effectively validating targets. The combination of AI and cloud computing is the perfect combination for many innovative purposes. With quick access to large amounts of data and big data, and cloud technology undoubtedly providing this, the success rate of various approaches such as AI's cognitive capabilities and machine learning will increase. Cloud adoption leads enterprises to AI as vendors offer more and more tools and services without large upfront investment. Clouds and AI are perfectly compatible in many ways, and experts say AI is just the technology that will revolutionize cloud computing solutions. AI is a type of know-how that has the potential to evolve today's cloud infrastructure and enhance the latest cloud computing technologies. Advances in AI and cloud technologies are helping healthcare and pharmaceutical companies improve their services

Conclusion:

Industry 4.0 indicates the new stage of the modernized industrial revolution with a high concentration on interconnectivity, flexible automation, artificial intelligence, and real-time data exchange and sharing using advanced technologies, such as cyber-physical systems, IoT, cloud computing, big data, and advanced robotics and virtual reality. Pharma 4.0 is a manifestation of Industry 4.0 in the pharmaceutical industry. Pharma 4.0 can be defined as the digitalization of pharmaceutical industries from the supply, production (with planning), and delivery operations` points of view by networked firms and uses intensively digital models and ontologies. The main missions of using this paradigm are to reduce the development costs and cycle time and to also improve the quality of the drug products by (a) improving the smartness of the contributing resources (i.e., humans, devices), (b) connecting and integrating all the contributing resources at any stage of the cycle, and (c) providing real-time status and awareness information to the regulatory organization. Pharma4.0 is powered by the cyber-physical platform, which enhances the processing of bigdata, maximizes the interconnectivity and collaborative robotics, and optimizes the artificial intelligence and distributed cloud architectures. This modern digitalization allows pharmaceutical and biotechnological organizations to change their network policies with higher efficiency and performance in different aspects. Networked embedded computers control and monitor the drug design, development, and production processes, usually with feedback circles from cloud-based computation unit. The economic and societal potential of the paradigm is vastly greater than what has been realized, and major investments should be made worldwide to develop the technology. The challenges are still considerable because pharmaceutical development and production systems should follow the tough instructions of the regulatory organizations to grasp safety and reliability requirements. Moreover, the tools used (i.e., PAT, QbD, RTRT) for the design, monitoring, and control of the drug production system are qualitatively different from other production industries. For example, the lack of temporal semantics and adequate concurrency models in computing and today`s “best-effort” networking technologies make predictable and reliable real-time performance difficult. Software component technologies such as object-oriented design and service-oriented architecture are based on software-like abstractions rather than physical systems. Many applications can only be achieved with significant changes to the core abstraction. The current drug development life cycle has the following problems:

- The drug development life cycle requires input from many contributors (devices, organizations, people, etc.). Participants employed in the drug development life cycle are not smart enough and unconnected.
- All decisions must be made by humans.
- This cycle is not integrated with the regulatory body. – This cycle is very long, costly and time consuming (12 years, B $ 2) The future drug development life cycle has the following benefits:
- All contributors are connected to cloud computing entities that have AI tools available and are ready for decision making. Contributors will be very smart.
- Contributors will cooperate. This will ignore duplicate processes.
- Regulatory tracking and tracking of medicines is much easier.

This chapter describes a series of phases of drug development, highlights the role of computers in drug development, and introduces the Pharma 4.0 ecosystem. Pharma 4.0 concludes that by increasing the level of intelligence, it may be possible to improve current drug design and development processes and validate manufacturing facilities. To realize Pharma 4.0 more effectively, we will rebuild new paradigms such as PAT (Process Analytical Technology), RTRT (Real-Time Release Testing), and QbD (Quality by Design) to reconstruct physical equipment and computing equipment. Must be covered in an integrated manner.

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