International Journal of Research in Engineering and Science (IJRES)
ISSN (Online): 2320-9364, ISSN (Print): 2320-9356
www.ijres.org Volume 10 Issue 9 ǁ September 2022 ǁ PP. 434-438

Energy Saving and Carbon Reduction Technology Transformation for Biopharmaceutical Industry: Taking Conba Company as an Example

Hua Wang and Jian Yu
School of Information and Electronic Engineering, Zhejiang University of Science and Technology, Hangzhou, China
Corresponding Author:Hua Wang

Abstract
The construction of this project meets the requirements of Conba Biopharmaceutical Company. It not only satisfies the needs of the relocation of fermentation and API (Active Pharmaceutical Ingredient) production lines to ensures the stable supply of relevant APIs, but also enhances the overall economic benefits of Conba and promotes the steady and healthy development of the enterprise. The relocation of API production line is necessary for planning compliance, as well as for the upgrading of product lines and industrial upgrading of the company. It is also necessary to comply with the laws and regulations related to safety and environmental protection. The construction and commissioning of the project will play a positive role in promoting the upgrading of the biopharmaceutical industry, protecting human health, increasing employment and increasing tax revenue. It will also help Zhejiang Province of China to set a benchmark for energy saving and carbon reduction in the pharmaceutical and chemical industry and drive the overall green transformation of the industry.
Keywords: *Energy saving and carbon reduction, Biopharmaceuticals, Relocation of API production line.*

Date of Submission: 05-09-2022 Date of acceptance: 20-09-2022

I. INTRODUCTION

The *Implementation Plan for Promoting the Relocation and Transformation of Enterprises of Hazardous Chemical Production in Densely Populated Urban Areas of Zhejiang Province in China* [1] and other documents require municipalities to speed up the relocation and transformation of hazardous chemical production enterprises in densely populated urban areas and promote industrial transformation and upgrading. Hazardous chemical production enterprises outside chemical parks that do not meet the safety and health protection distance requirements must be transformed to meet the standards, relocated into regulated chemical parks or closed down before 2025. At the same time, according to the deployment of the carbon peak work of Zhejiang Province, pharmaceutical and chemical enterprises must speed up the upgrading of products and green technology transformation of production methods to promote the industry's carbon emissions to reach the peak.

The leading products of Conba Bio-Pharmaceutical Company [2] are*Aloxin*, *Jin Aokang*, *JinKang Puli* and *Amikacin Sulfate,* which have been awarded as *National Key New Product*, *Provincial High-tech Product*, *Famous Brand Product*, *New and Excellent Product*, *Junmai New and Excellent Products*, *Junma Award* and other awards. Several of APIs(Active Pharmaceutical Ingredient) and preparations have passed the cGMP of EU, FDA of US and WHO certifications. At the same time, the company has built three R&D platforms, which are the National Chiral Drug Zhejiang Branch Centre, the National Formulation Engineering Centre Zhejiang Branch and the Provincial Technology R&D Centre.

Conba now has production bases such as Jin Qulu and Jinxi. The bases are strategically adjusted to the product layout according to the government's planning and layout adjustment, so that the limited three types of land are used for chemical synthesis production, whichsatisfies the government and regulations on low-carbon and green requirements, and a reasonable allocation of resources is essential. The company has a total of nine raw material workshops, two extraction workshops and one fermentation workshop, including raw material workshops I, IV and VI. After digital transformation, the automated production line is undergoing trial production. Raw material workshop V has completed equipment commissioning immediately and can be organized for trial production. Other workshops are gradually carrying out the installation and commissioning stage of the automation control equipment. The company continues to promote the application of intelligent equipmentand flexible production lines in the workshops over the next two years, combining incoming material, extraction and fermentation technologies in the process flow with intelligent connection technologies to enhance the degree of automation. At the same time, the fermentation and API from the Jinqu Road site will be relocated to the site where the formulation production line was originally planned for the Jinxi International Advanced Pharmaceutical Base. The formulation production line is implemented at the Jinqu Road base. Thus, the Jinxi base becomes the API base and the Jinqu Road base is updated as the formulation manufacturing centre, R&D centre and logistics centre, responding strongly to the requirements for scientific planning and layout of the chemical industry at the Zhejiang Province level.

II. THE PROPOSED METHOD

A variety of wireless industrial equipment sensors are used to collect data to achieve timely and accurate reporting of all equipment operating data and fault data to the cloud platform. Incoming equipment is monitored online, offline, power and operating parameters of the equipment in real time through adapters. Through the analysis of the reported information, the real-time or stage power consumption and working time of the equipment are counted. Employing IoT technology and equipment monitoring technology to master the key production parameters of the equipment, the data analysis improves the utilization rate of the operating equipment and reduces unnecessary energy consumption. The use of IoT technology [3], MES manufacturing execution systems [4], SCADA(Supervisory Control And Data Acquisition) systems [5], could have a clear grasp of the production and marketing process to improve the controllability of the production process. The project reduces manual intervention and collecting the correct data on the production line in real time. Together with new technologies such as green and intelligent means and smart systems, we are able to build an energy efficient, green and environmentally friendly factory with a comfortable environment.

At the same time, the environmental problems associated with the current production situation at Conba must be improved in order to achieve savings and reductions in consumption. Low carbon management of the life cycle of pharmaceuticals emphasises low carbon and environmental protection in all aspects of research and development, production, distribution, use and recycling (disposal). At the front end of the pharmaceutical lifecycle, low carbon is mainly reflected in green chemistry. At the compound screening stage, R&D pharmaceutical companies pay attention to the selection of chemical structures that are more easily degradable. In the process design, synthesis steps and fermentation time are shortened as much as possible, and in the formulation, lyophilisation curve time is shortened and the application of excipients is reduced. The use of environmentally hazardous chemicals is also reduced throughout the production process.

2.1 CONSTRUCTION CONTENT AND SCALE

Based on big data, network and massive computing, the three elements of computing, communication and control are organically integrated and deeply collaborated by means of core intelligent logic judgement, analysis, mining, evaluation, prediction, optimization, collaboration and other technical means. The system is designed in a layered structure, and divided into three layers: the equipment layer (adapter), the data support layer (cloud platform) and the application layer. Equipment data is collected centrally and SCADA covering the production line is established to meet the requirements of GMP regulations on production data collection and storage, which solves the problem of data silos and achieves a high level of data integration under a unified platform. To achieve data integrity and traceability and to provide data for MES and other systems. According to the characteristics and requirements of the production process, the main parameters of the process, the system involves temperature, pressure, level, flow, weighing, flammable gas and equipment operation status, which can be displayed, recorded, adjusted, accumulated, controlled, chained, alarmed, printed and online modification of the set parameters. Through the implementation of the DCS (Distributed Control System) [6], the equipment is basically controlled automatically by PLC (Programmable Logic Controller)[7] for the stations and the whole production process is controlled automatically. The installation of monitoring and warning facilities at key production, storage and use sites of hazardous chemicals has the significant advantage of saving investment and low energy consumption.

The project will be relocated to the second phase of Conba Jinxi International Advanced Pharmaceutical Base, and approximately 36 mu of land on the southeast side of the base will be added as the site for the relocation project. The API production line in the Jinqu Road plant will be relocated to the Phase II site of the international advanced pharmaceutical base of the project. At the same time, in order to rationalize the use of production line resources and ensure a controlled supply chain, a new production line for kanamycin and a production line for tazobactam acid intermediates is built.

2.2 ADOPTION OF PROCESS SOLUTIONS

The hydrochloric acid, daikonomycin sulphate and kanamycin products are fermented and extracted products in the project. Among them, the key fermentation and extraction technology has independent intellectual property rights, using common raw materials to achieve energy saving and cost reduction. The use of new solvents and reagents reduces the difficulty of producing and treating the *Three Wastes* [8], makes it easy to industrialize production and reduces environmental pollution while industrialization production. Taking daikonomycin hydrochloride as an example, the main production process is as illustrated in Figure 1.

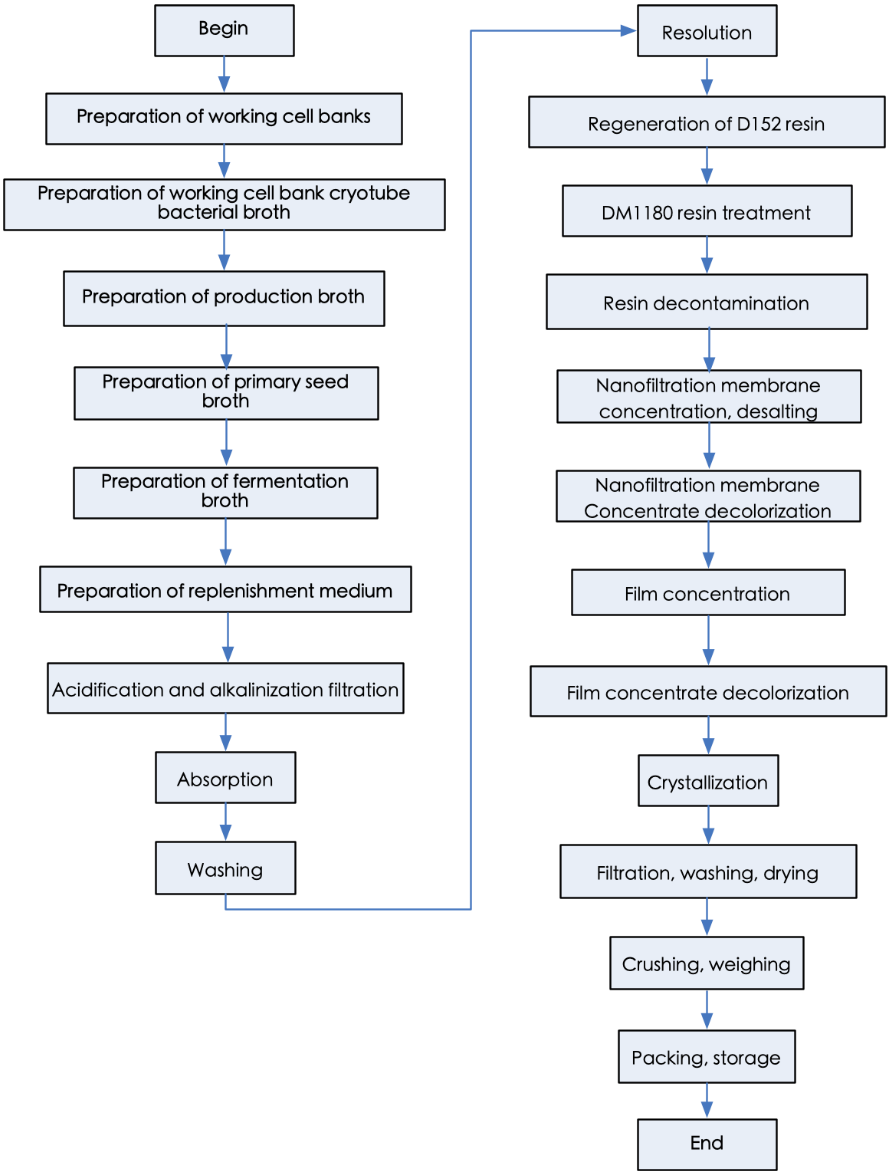

Figure 1: Taking daikonomycin hydrochloride as an example, the main production process

2.3 PRODUCT PROGRAMME

(i) Daikanomycin hydrochloride: the molecular formula $C_{14}H_{24}N_2O_7 \cdot 2HCl \cdot 5H_2O$, easily soluble in water, almost insoluble in ethanol, trichloromethane or ether. In recent years it has been widely used in Europe, America and the domestic veterinary market, mainly for bacterial infections in livestock and poultry, marine and freshwater fish and other aquatic animals. Also, it is an antibiotic permitted for use in the production of Grade A green foods as stipulated in China.

(ii) Spectinomycin Sulphate:the molecular formula $C_{14}H_{24}N_2O_7 \cdot H_2SO_4 \cdot 4H_2O$, is soluble in water and insoluble in ethanol, ether and chloroform. It is the drug of choice and a potent drug in the treatment of gonorrhoea today and has a strong inhibitory capacity against both gram-negative and positive bacteria and mycobacteria.

(iii) Kanamycin:the molecular formula $C_{18}H_{36}N_4O_{11}$, is a protein biosynthesis inhibitor that can be used orally and intravenously and is effective against a wide range of pathogenic infections.

(iv) Amikacin sulfate: the molecular formula $C_{22}H_{43}N_5O_{13} \cdot 2H_2SO_4$, is almost odourless and tasteless. It is extremely soluble in water and almost insoluble in methanol, acetone, ethyl ether or trichloromethane. It is a semi-synthetic aminoglycoside antibiotic with a wide antibacterial spectrum and has strong antibacterial ability against many kinds of bacteria, especially good therapeutic effect against mycobacterium tuberculosis.

(v) Tazobactam acid: the molecular formula $C_{10}H_{12}N_4O_3S$, is odourless, bitter in taste; slightly hygroscopic. It is the most clinically effective β-lactamase inhibitor with high stability, low activity, low toxicity and strong enzyme inhibiting activity.

2.4 MAIN EQUIPMENT SELECTION AND ENGINEERING SOLUTIONS

The plant area is lined with a green belt along the inside of the fence, on both sides of the road. Turf and some resistant shrubs can be planted around the buildings. In the vicinity of the workshops, grease-free and non-fluttering trees with fire protection are planted. Emphasis is placed on strengthening the landscaping design of the green belt in the front area of the plant and along the side of Weisi Road, as well as the protective greening design around the three waste treatment areas. The vertical layout is flat-sloped and the site is drained by open ditches. Rainwater is collected by the rainwater pipe and discharged to the municipal rainwater pipe outside the plant. Wastewater is collected in the workshops or warehouses and then transported to the three waste treatment areas through the external pipe corridor and then discharged to the municipal sewer outside the plant after reaching the standard.

2.5 MAJOR ENERGY-USING EQUIPMENT AND ADVANCED EVALUATION

The production equipment used in this project is the most advanced domestic equipment used in conjunction with foreign equipment.

(1) LGZ type vertical automatic scraper lower discharge centrifuge [9]: is a new model designed and manufactured in accordance with GMP specifications for pharmaceutical equipment. Equipped with fully enclosed openable cover, flat plate machine base, frequency conversion speed control. It is fully enclosed and explosion-proof, with a high degree of automation, large processing capacity, good separation effect and in accordance with GMP standards. It is suitable for separating suspensions containing solids with a particle size greater than 0.05mm, and is especially suitable for separating materials that are not suitable for personnel to approach.

(2) SZG double cone rotary vacuum dryer [10]: It is a new generation drying device developed by combining the technology of similar products in China, with belt and chain two-stage flexible linkage, thus the equipment runs smoothly. On the basis of this, it can both steplessly adjust the speed and carry out constant temperature control. It is suitable for the concentration, mixing and drying of powder, granular and fibrous materials in the chemical, pharmaceutical and food industries, as well as for the drying of materials requiring low-temperature drying, and is also suitable for the drying of materials that are easily oxidized, volatile, heat-sensitive, strongly stimulating, toxic and materials that do not allow the destruction of crystals.

(3) GLZ Series Vacuum Screw Dryer [11]: It is a combination of drying, crushing, vacuum decompression and powder mixing, consisting of reducer, screw agitator, conical cylinder with jacket heating and discharge valve, etc. It can realize the whole process as closed continuous operation, and its drying efficiency is 3~5 times of double cone rotary vacuum dryer of the same specification.

(4) Other energy-consuming equipment: The project has a large demand for compressed air, and the main air-using workshop is the fermentation workshop, followed by valves and instruments. In order to reduce the leakage and pressure loss of compressed air pipeline, and to improve the efficiency of energy consumption, the fermenter mixing motor (132KW*24 sets) and air compressor motor (810KW*4 sets) of the power-consuming equipment of the project adopt ultra-high efficiency motors, which enable them to run at low temperature and have a long service life. Motor efficiency can be increased from 93% to 96.5%, saving 1.6 million kWh of electricity. At the same time, the motor drive of this project is extensively controlled by frequency conversion, which can save 1.7 million kilowatt-hours of electricity.

In addition, the steam of this project is supplied by the steam pipe network of the park, and the peak steam consumption is expected to reach 36t/h. In order to meet the demand for energy saving, the adoption of high efficiency continuous elimination system and other technologies and equipment can save 70% of the steam used for sterilization and sterilization, and the annual saving of steam consumption is 19,644t.

III. CONCLUSION

After the relocation of the project, the annual electricity consumption of daikonomycin and amikacin sulfate is 20.69 million kWh, the annual steam consumption is 61,856t, the annual water consumption is 420,000m^3, and the comprehensive energy consumption equivalent value will be 11,748.09tce. Before the relocation, the annual electricity consumption was 24.21 million kWh, the annual steam consumption was 81,500t, the annual water consumption was 435,000m^3, and the comprehensive energy consumption equivalent value was 14,594.95tce. Compared with the pre-relocation target, the annual electricity consumption of the project is 3.517 million kWh, the annual steam consumption is 19,644t, the annual water consumption is 15,000m3 , and the annual comprehensive energy consumption (equivalent value) is 2,846.86tce.

3.1 ENVIRONMENTAL BENEFITS

(i) Exhaust gas emissions: After the proposed project is completed and put into operation, clean production processes is adopted. The project have a low impact on the local ambient air and ecosystem as the pollutants is discharged after effective treatment during the production process.

(ii) Wastewater discharge: The wastewater generated by the project is pre-treated in the plant and then discharged into the Qujiang River after being treated to satisfy the standard of wastewater treatment plant, which has no impact on the surface water environment of the project site.

(iii) Solid waste disposal The solid waste generated in the production process of the project is classified and safely disposed of. The various disposal measures not only reduce the external emissions of waste, but also minimize the pollution to the environment.

(iv) Noise control: After the project noise adopts measures such as sound insulation and vibration damping, the impact on the perimeter environment of the plant area is reduced and the perimeter sound environment can be maintained as it is. The project has achieved the standard discharge of wastewater through clean production and pollution treatment. The separation of clean sewage flow and the treatment of wastewater up to the standard not only prevent the pollution of inland rivers, protect the regional surface water quality and aquatic environment, but also protect the health of the public and economic benefits. The project's clean production process minimizes the discharge of pollutants with minimal impact on human health and agro-ecology in the region. The comprehensive use of homogenous waste and safe external disposal mitigate the impact on the surrounding water bodies, ambient air, soil and other environments.

3.2 SOCIAL BENEFITS

The project firmly implements and enforces relevant national and local policies and regulations on environmental protection. The project adopts advanced production technology and reasonable measures for the treatment of the *Three Wastes*. Based on the comprehensive intelligent management and production system, it effectively reduces the amount of *Three Wastes* generated and the difficulty of treatment, meeting the requirements of clean production and environmental protection. The construction and operation of the project will play a positive role in promoting the level of public health, upgrading the biopharmaceutical industry and protecting human health in Zhejiang Province of China.

Through the construction of this project, the company establishes a production line for APIs that complies with Chinese GMP and European and American GMP, and will effectively combine advantageous products of the company. At the same time, the company's technology and equipment are significantly upgraded on the existing basis, with particular emphasis on improving safety management and environmental protection. The company becomes an internationally advanced pharmaceutical enterprise with exemplary standards in the industry, thus enhancing the overall image of the company.

REFERENCES

[1]. Chen Qingjun, Li Qiang. (2019)"Optimization of implementation plan for relocation and transformation of hazardous chemical production enterprises in densely populated urban areas (in Chinese)" Chemical Industry, Vol.37, No.5, Pp.5-10.

[2]. www.conbapharm.com:9443/en, (2020).

[3]. Chemical, Weekly, & group. (2016). "IoT in chemical industry" Chemical Weekly, Vol.61, No.35, Pp.202.

[4]. Sm, A. , & Cm, A. . (2019). "An overview of next-generation manufacturing execution systems: how important is mes for industry 4.0?" Procedia Manufacturing, Vol.30, Pp.588-595.

[5]. Zand, A.D., Khalili-Damghani, K. & Raissi, S. (2021) "Designing an Intelligent Control Philosophy in Reservoirs of Water Transfer Networks in Supervisory Control and Data Acquisition System Stations" Int. J. Autom. Comput. Vol.18, Pp.694–717.

[6]. Chen, Sq., Su, H. (2000) "Design of a developing platform of supervisor and management system for industrial process in DCS based on client/server architecture" J Cent. South Univ. Technol. Vol.7, Pp.97–99.

[7]. Kovalenko, Y. (2017). "A Programmable Logic Controller (PLC); Programming Language Structural Analysis" In: Recent Advances in Systems, Control and Information Technology. SCIT 2016. Advances in Intelligent Systems and Computing, Vol. 543. Pp. 234–242.

[8]. Feng Zhichong, Zhang Yue, Zhuang Yingping, et al. (2021)"Integrating green engineering education to help the harmless treatment of *three wastes* in the laboratory" Laboratory Research and Exploration, Vol.40, No.3, Pp.4-14.

[9]. Chemical, Engineering, World, & group. (2017) "Bottom discharge centrifuge with scraper" Chemical Engineering World.

[10]. Huang, H. , & Amp, H. C. . (2014). "Application of wireless instrument in vacuum rotary dryer". Automation in Petro-Chemical Industry.

[11]. Merkle, U. . (2020). "Dry vacuum technology for chemical and pharmaceutical processes notes for the use of screw vacuum pumps" Chemicalplants processing.