Study on Resource Utilization of Biopharmaceutical Residue Based on Membrane Separation Technology

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Abstract: Biopharmaceutics is a kind of organic resource that uses protein, starch, vitamins, minerals and other raw materials to produce drugs through microbial fermentation. Its residue contains rich mycelium and residual organic and inorganic substances. Bio-pharmaceutical residue is one of the most serious pollution sources in bio-pharmaceutical enterprises. Over the years, some enterprises have tried to reuse the residue and achieved some results, but most of them are directly discharged as waste, bringing pollution to the surrounding environment. Biopharmaceutical fermentation is a hot topic in the research of biopharmaceutical modernization in recent years. It is a perfect combination of modern biotechnology and traditional biopharmaceutical advantages, and is one of the important means to improve the material basis of biopharmaceutical efficacy. Based on membrane separation technology, this paper focuses on bio-fermentation of bio-pharmaceutical residues, and reviews from aerobic fermentation and anaerobic fermentation, which provides new ideas for the deep development of bio-pharmaceutical residues and the sustainable utilization of bio-pharmaceutical resources.

1. Introduction

In recent years, China's economy has developed rapidly, but at the same time it has also paid huge resources and environmental costs. The contradiction between development and resources and environment has become increasingly prominent. The country is paying more and more attention to the rational use of resources. With the rapid development of China's biopharmaceutical industry, the amount of waste of biopharmaceutical residues from major biopharmaceutical factories in the country is increasing day by day, with annual emissions reaching 30 million tons [1]. How to effectively treat and utilize the residue is of great significance for saving resources, preventing environmental pollution and developing circular economy. Therefore, how to effectively make rational and comprehensive use of biopharmaceutical residues so as not to pollute the environment but to better serve human beings has become one of the problems that many scholars have been scrambling to study and solve [2]. Based on membrane separation technology, this paper focuses on the microbial fermentation of biopharmaceutical residues from two aspects of anaerobic fermentation and aerobic fermentation, in order to provide reference for the further development of biopharmaceutical residues and the sustainable utilization of biopharmaceutical resources.

2. Application of Membrane Separation Technology in Development of Bio-Pharmaceutical Residue

Application of membrane separation technology in antibiotic extraction. Antibiotics in the traditional production process, the process is relatively lengthy, to be filtered, extracted, concentrated, crystallized and many other steps, while the application of membrane separation technology can make the process easier. Cross-flow filtration separation of bacteria by microfiltration or ultrafiltration is one of the important applications of membrane separation. Nanofiltration membrane has a unique function in the separation of low-valence ions and high-valence ions, so nanofiltration is more suitable for the purification and softening of water and the removal of organic matters and heavy metals in water. The membrane process can be divided into

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microfiltration, ultrafiltration, nanofiltration, reverse osmosis, pervaporation, dialysis, electrodialysis, gas separation, etc. according to the different components retained. In other words, the general charge-type separation membrane has almost no interception effect on the amino acid and polypeptide solute in the peer state, but has a higher interception effect on the amino acid and polypeptide solute in the point state. Improving the hydrodynamic conditions of the membrane can reduce the polarization degree of concentration difference and improve the permeation flux of the membrane.

Anaerobic fermentation is also called anaerobic digestion, which refers to the process that anaerobic microbial flora converts organic matters in solid waste into CO2, CH4 and its own material energy under anaerobic conditions. The crude drugs of biopharmaceuticals are protein, starch, minerals, vitamins, etc. After pharmaceutical fermentation, the main components of the residue are residual raw materials and generated mycelium. Edible fungus polysaccharide has many effects, such as anti-tumor, anti-virus, regulating immune activity, promoting nucleic acid and protein biosynthesis, improving human metabolism, strengthening body constitution, regulating plant nerve function, etc. In this way, not only can the traditional cottonseed hull cultivation materials be gradually lacking, but also the nutritional value of the cottonseed hull cultivation materials is beneficial to the improvement of the nutritional value of edible fungi. Various inorganic elements, organic acids, cellulose and the like remained in the residue can provide rich nutrition conditions for the growth of anaerobic bacteria. The experimental results showed that the biotransformation rate of Pleurotus ostreatus cultivated with bio-pharmaceutical residue as the main material and a reasonable proportion of sawdust, bran and other substances was significantly higher than that of cottonseed hull. The residue after environmental protection treatment, through drying and analysis of the dried residue, shows that the bio-pharmaceutical residue is rich in a variety of organic substances, and no heavy metal mercury is detected. It is a very high-quality organic matrix material.

3. Approaches to Resource Utilization of Bio-Pharmaceutical Residue

3.1 Prepare Organic Fertilizer

Biopharmaceutical residues often contain a certain amount of active ingredients and a large amount of crude fiber, crude fat, starch, crude polysaccharide, amino acids and inorganic nutrients, and are one of the best raw materials for producing bio-organic fertilizer. Bio-pharmaceutical residue contains a large amount of natural macromolecular substances, which have certain flocculation effect on organic wastewater. Qu et al. [3] The organic fertilizer made from bio-pharmaceutical residue, corncob and clay as raw materials and sawdust as carrier of fermentation broth after a series of processing treatments has a high content of organic matter, which can improve soil properties, improve soil fertility and promote plant growth. It is converted into thermal degradation of small molecular substances. The pyrolysis process finally produces three products: liquid bio-oil, combustible gas and solid bio-carbon. The proportion of products varies according to different pyrolysis processes and reaction conditions.

By monitoring the fermentation temperature, the stack can be turned over, not only sufficient oxygen can be supplied into the stack to promote the fermentation and decomposition of the materials, but also the materials can be stirred evenly to enable the surface materials to turn over to the inside, and at the same time, disease microorganisms, disease eggs and the like can be completely killed through aerobic microorganism high-temperature fermentation to achieve the purpose of harmless treatment. The organic matter content, total nutrients, total phosphorus content and pH value of the prepared organic fertilizer product are shown in the following table.

The residue enters the primary fermentation chamber after pretreatment. the horizontal rotary fermentation drum adopted in this scheme can effectively control the fermentation parameters, thus adjusting the fermentation state, shortening the fermentation period by 2-3 days, and greatly improving the fermentation efficiency. Lu [4] takes bio-pharmaceutical residue as the main raw material, and the ganoderma lucidum solid fungus cultured by solid fermentation method contains rich bioactive components, and has low heavy metal content and little toxic and side effects. The prepared fertilizer product not only contains organic matter, but also contains rich nutrients of inorganic components of nitrogen, phosphorus and potassium, and is an organic fertilizer with comprehensive nutrition, high efficiency and no pollution.

Table 1 Organic Fertilizer Standard

Projects	organic content	Total nutrient($N+P_2O_5+K_2O$)	Total phosphorus	pH
Organic fertilizer produced	39.6%	6.3%	1.36%	7.2
Ministry of agriculture standard	≥30%	≥4.0	≥1.84	5.8-8.0

3.2 Bio-Pharmaceutical Residue is Used for Edible Fungus Cultivation

The method for cultivating edible fungi with biopharmaceutical residue comprises pouring the biopharmaceutical residue into a clean plastic bag while it is hot, cooling to room temperature, spraying liquid strain, and culturing to grow edible fungi. After edible fungi are cultivated with bio-pharmaceutical residue, the residue can be further fermented to prepare organic fertilizer, thus realizing zero discharge of the residue and the residue, bringing great economic benefits, social benefits and environmental benefits, and realizing economic circulation. Qu et al. [5] used bio-pharmaceutical residue and vinegar residue as nutrients for cultivation of ganoderma lucidum. as a result, the yield and biological efficiency of ganoderma lucidum cultivated with vinegar residue combined with the same amount of bio-pharmaceutical residue can reach or even slightly exceed that of pure cotton seed hull control group, and its hypha is white, dense and thick. The antioxidant activity of fermented products is higher than that of unfermented products, and the fermented products have broad-spectrum antibacterial activity against pathogenic bacteria, which provides a theoretical basis for bio-fermentation to enhance the release of active ingredients in bio-pharmacy. Biopharmaceutical residue waste with high plant fiber content is a potential raw material for pulping and papermaking industry. Combining the two can not only relieve the shortage of pulping raw materials to a certain extent, but also reduce the burden on the environment and protect forest resources. Song et al [6] used bio-pharmaceutical residue mixed with other ingredients to conduct screening tests on the formula of culture medium for cultivating Pleurotus ostreatus. The results showed that when bio-pharmaceutical residue and vinegar residue were used as cultivation base materials, the growth condition of Pleurotus ostreatus was stable and the yield was increased. After the enzymatic decomposition of edible fungi, it is rich in nitrogen, phosphorus and potassium, which are essential for plants, and can also be used as high-quality natural organic fertilizer. Therefore, the author believes that it is one of the preferred methods for the treatment of bio-pharmaceutical residues.

3.3 Livestock Feed

The bio-pharmaceutical residues not only contain rich nutritional ingredients, which can promote the growth of poultry storage, but also contain some medicinal ingredients, which have certain preventive and therapeutic effects on the prevention and treatment of poultry storage diseases. It is mainly fermented biological feed. The fermented biological feed is characterized by sour and sweet smell, good taste, lower equipment and technical requirements, simpler decomposition of macromolecular substances in the feed, easy preservation of protein, golden appearance of the feed and good sales. Su et al. [7] In the research on the production of medicinal fungus polysaccharide biological feed by fermentation of salvia miltiorrhiza residue, the mixed fermentation of salvia miltiorrhiza residue by multi-strains mainly composed of medicinal fungus showed that the contents of soluble polysaccharide and true protein after fermentation were significantly increased compared with those before fermentation. The fermentation and decomposition process of preparing organic fertilizer from bio-pharmaceutical residues mainly uses aerobic microorganisms for high-temperature fermentation and harmless and stable treatment of materials. Cheng et al. [8] studied the effect of bio-pharmaceutical residue combined with rabbit diet on its growth. The residue mainly used was Codonopsis pilosula, etc. The results showed that compared with the control group, the feed group added bio-pharmaceutical residue had higher economic benefits, lower feed consumption and higher daily gain. It is also a promising treatment method to convert bio-pharmaceutical residue into poultry storage feed. In particular, the use of biotechnology to convert residue into high protein thallus protein feed through microbial fermentation can greatly improve the utilization value of residue and increase added value.

3.4 For Wastewater Treatment

The bio-pharmaceutical residue can be used for cultivation of edible fungi, trial production of organic fertilizer, feed or additive, and treatment of organic wastewater. He et al [9] used bio-pharmaceutical residue as flocculant to treat papermaking wastewater, and compared with inorganic flocculant and organic flocculant, it was found that self-made bio-pharmaceutical residue had good flocculation effect, and bio-pharmaceutical residue as natural polymer flocculant was simple to prepare and had good treatment effect on papermaking wastewater. Zhang et al [10] used isatis root residue to treat low-concentration lead-containing wastewater. the results showed that isatis root residue can rapidly adsorb a large amount of lead, and has higher adsorption rate and faster adsorption speed for low-concentration lead solution. Zhang et al [11] used endoglucanase and total cellulase as the activity indexes to investigate the effects of fermentation time and water activity on the production of cellulase in the experiment of investigating the production of cellulase by Aspergillus niger solid-state fermentation of red jujube residue. It has a uniform pore diameter adjustable between 2nm and 50nm, and its specific surface area is over 700 m^2/g. Due to its remarkable advantages, it has broad application prospects in the fields of catalysis, adsorption, materials, etc. The bio-drug residue can rapidly adsorb lead element in wastewater, and the adsorption speed is accelerated and the adsorption speed for low-concentration lead solution is higher, thus achieving the purpose of reducing the content of lead element in industrial wastewater.

4. Prospect and Prospect of Utilization of Bio-Medicine Residue Resources

With the rapid development of biopharmaceutical industry, the gradual improvement of industrial level and the continuous expansion of production scale, the secondary utilization and in-depth development of biopharmaceutical residues can guide the biopharmaceutical industry onto the road of green and sustainable development. However, there are also many problems in the use of bio-pharmaceutical residues. Due to the diversity of sources and the complexity of components of bio-pharmaceutical residues, their safety should be fully considered in reuse. For example, it is necessary to determine whether edible fungi contain toxic substances in order to avoid serious consequences after people eat them. As a cultivation substrate, three criteria should be met: most of the easily decomposable organic matters are decomposed; Biological fixation that does not produce nitrogen during cultivation and use; Harmful compounds such as phenolic acid and the like are removed through degradation, and pathogenic bacteria, eggs and weed seeds are eliminated. Plant fiber resources are different from non-renewable resources such as petroleum resources. Their renewable and degradable characteristics deserve our attention. For example, the dregs are easy to pollute the surrounding environment due to rain during the stacking process, especially in areas with shallow groundwater level. As a commodity circulating on the market, the organic cultivation substrate must have a fixed formula, stable ingredients and reliable performance, be suitable for packaging and transportation, be easy to use in quality, be non-toxic, harmless, odorless, and have good biological stability. China is rich in bio-pharmaceutical residue resources. Therefore, bio-pharmaceutical residue reuse has great prospects, which will not only achieve good economic benefits, but also achieve good social benefits.

5. Conclusion

Membrane separation technology has the advantages of simple equipment, convenient operation, no phase change, no chemical change, high treatment efficiency and energy saving. With the further development of membrane technology, group structure and equipment development. The reasonable utilization and treatment technology of the residues produce edible fungi, produce bio-organic fertilizer, use the residues as biomass gasification raw materials, etc., which not only popularize the production technology of pollution-free agricultural products, but also achieve better ecological, economic and social benefits, which is of great significance. The treatment of bio-pharmaceutical residues is also a complicated and arduous task. It is only a beginning in China and there is still a lot of work to be done. In the utilization and treatment of the residues, we should make full use of the residue resources on the one hand, and on the other hand, we should prevent secondary pollution and protect our living environment.

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