APPLICATION OF MEMBRANE SEPARATION IN BIOTECHNOLOGY

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ABSTRACT

Membrane technology emerges as one of the most important separation methods, which have captured the attention of industries, related to biochemical, pharmaceutical, biomedical, and food industries. Due to the current intensive development and expansion, membrane technology is also rapidly gaining market recognition and application in Malaysia. Factors accelerating the positive growth of membrane market in Malaysia include economic factors, technology, support industries and awareness in environmental safety and health. Therefore, this paper seeks to review the separation mechanism, advantages and applications of synthetic polymeric membranes in biotechnology.

Key words: Membrane, dialysis, reverse osmosis, ultrafiltration, microfiltration

INTRODUCTION

In recent years, membranes have gained wide acceptance and made significant inroads against competing technologies in many areas including biotechnology, because of flexibility and performance reliability of membrane system, cost competitiveness, increasing demand and environmental awareness. According to Gaden's definition, biotechnology comprises all aspects of technological exploitation and control of living systems; while bioprocesses involve the use of complete living systems or their components in a directed and controlled manner to bring about desired physical or chemical changes [1]. In biotechnology, membrane system could be potentially suitable for treating the dilute solutions and finely dispersed solids, especially those which are compressible, have a density close to that of the bulk phase, have high viscosity, or are gelatinous (colloidal suspensions); low molecular weight, non-volatile organics or dissolved salts; pharmaceutical and biological materials which are sensitive to their physical and chemical environment. Membrane processes that are successfully commercialized in biotech industry include dialysis, electrodialysis, reverse osmosis, ultrafiltration, microfiltration and etc. These membrane processes can differ greatly in their area of application, structures of membrane and operating principles. There is always a degree of arbitrariness about such classifications, which is summarized in Table 1 [2]. Indeed, the opportunities of membrane technology in bioseparations are immense, with inroads continually being made in new fields.

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Table 1: Important Membrane Separation Processes in Biotechnology

Separation Process	Membrane Type	Driving Force	Method of Separation	Range of Application
Microfiltration	Symmetric microporous membrane 0.1μm to 10μm pore radius	Hydrostatic pressure difference 0.1bar to 1bar	Sieving mechanism due to pore radius and absorption	Sterile filtration clarification
Ultrafiltration	Asymmetric microporous membrane 0.1μm to 5 nm pore radius	Hydrostatic pressure difference 0.5bar to 5bar	Sieving mechanism	Separation of macro-molecular solutions
Reverse Osmosis	Asymmetric "skin type" membrane	Hydrostatic pressure difference 20bar to 100bar	Solution-diffusion mechanism	Separation of salt and microsolutes from solutions
Dialysis	Symmetric microporous membrane 0.1nm to 10nm pore radius	Concentration gradient	Diffusion in convective free layer	Exchange of dissolved solutes and solvent from solutions
Electrodialysis	Cation and anion exchange membranes	Electrical potential gradient	Electrical charge of particle and size	Desalting of ionic solutions

FUNDAMENTALS OF MEMBRANE SEPARATION PROCESS

A membrane acts as a selective barrier and restricts the transport of various chemical species in a rather specific manner due to its properties and the force field applied [3]. For a separation process, one of the streams would be the feed solution. The separation intrinsically relies on a kinetic phenomenon; the components that can quickly permeate through the membrane are effectively separated from those that permeate at a slower or negligible rate [4]. As the feed stream flows past the membrane, the outlet stream is thus concentrated in the slowly penetrating species and leaves as the retentate, while the permeate is enriched in the quickly penetrating species. Membrane processes rely on certain driving forces to achieve the transport of species through the membrane, including the concentration, pressure, or electrical gradients [3]. The feasibility of a given membrane separation depends on both the achievable product purity and production rate [4]. The former is important for product specifications and the latter for economic reasons. The production rate at which a given material may be recovered is governed by the flux through the membrane, while the product purity and total product recovery are governed by the selectivity of the membrane.

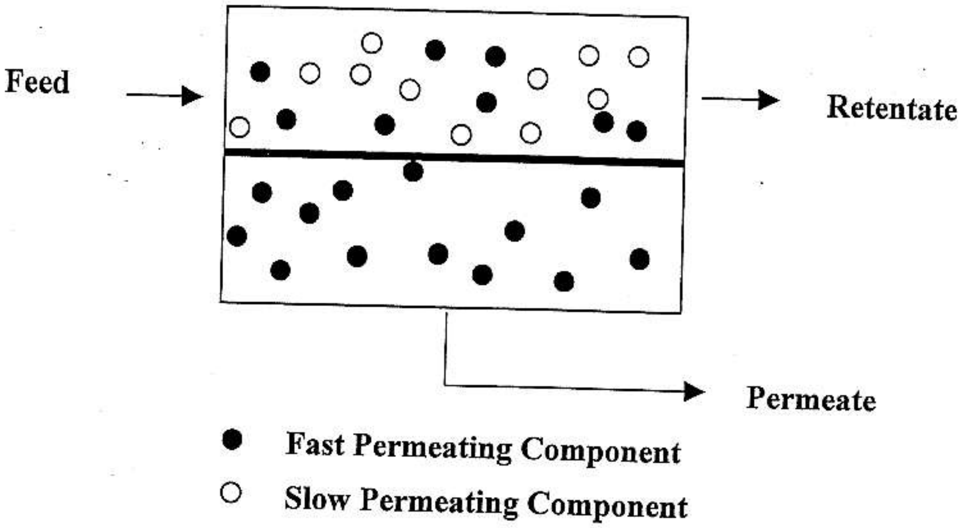

Figure 1: Schematic Diagram for Membrane Separation

ADVANTAGES OF MEMBRANE SEPARATION SYSTEM

The history of synthetic polymeric membranes is now slightly greater than a century old [3, 5]. Recently, membrane separation process has become increasingly important and popular in industries and have displaced conventional separation methods such as absorption, distillation, liquid-liquid extraction, leaching, crystallization and adsorption etc. because of its inherent efficiencies and benefits in applications, stated as following:

(i) Membrane systems are economical viable and flexible. The capital investment and production costs of most membrane systems are about 30% to 40% lower than the corresponding conventional systems.

(ii) Membrane devices and systems are almost always compact and modular, especially if the membrane is provided in the form of a bundle of hollow fibers and spiral wound, which occupy high area per unit volume [6]. This factor also leads towards weight and space efficient which is important in transportation or offshore platform applications.

(iii) Membrane systems can be operated in mild conditions and simple process equipment is required. Furthermore, isolation of the facility or requirement of personnel is also reduced due to the mechanically simplicity and maintenance free of membrane systems [7].

(iv) Membrane systems are energy efficient since there are large reduction in power (electricity and fuel) consumption for the systems. Utilities usually will not be necessary unless compression is needed, and no rotating parts or circulating liquids is involved [8].

(v) Membrane separation technology is safe and their environmental impact is low because they contain no toxic material and are compact in size. This environmental-friendly unit operation also brings no pollution or hazards to the nature compared with other conventional separation methods [9].

(vi) The separation with membranes is usually performed at ambient temperature; thus a temperature-sensitive solution can be treated without the constituents being damaged or chemically altered. This is important for mass separation problems in the food and drug industry and in biotechnology, which often require processing of temperature-sensitive products [10].

APPLICATION OF MEMBRANE PROCESSES IN BIOTECHNOLOGY

Filtration

The most widely used membrane technique in the separation of biological molecules from solution is filtration process, which includes reverse osmosis, ultrafiltration and microfiltration. These processes are used to separate solute and solvent components in a solution. However, these pressure-driven membrane filtration processes form a continuous sizing spectrum. Microfiltration (MF) membranes retain particulates such as microorganisms and are rated according to pore size, usually from 100 nm to several micrometers [1, 11]. Ultrafiltration (UF) membranes retain macromolecules and are rated either by pore size (1 nm to 100 nm) or molecular weight cutoff, typically from 1,000 to 1,000,000 [1, 11]. Reverse osmosis (RO) membranes retain low-molecular-weight solutes with pore size < 1 nm [1, 11].

Nowadays, reverse osmosis has been widely applied in producing drinking water from seawater (> 800 psig) and brackish water (> 300 psig) suitable for industrial or domestic applications, which is also known as seawater desalination. Reverse osmosis membrane allows water molecules to pass through freely, but filters out dissolved salts, ions and organic solutes such as nitrates, bacteria and viruses. The preferential sorption of water molecules at the solvent-membrane interface caused by the interaction among the membrane, solvent, and solute molecules is responsible for the separation. The most important reverse osmosis membranes are cellulose acetate (CA), cross-linked polyamide (PA) thin film composite (TFC), and linear aromatic polyamide hollow fiber [12]. Both cellulose acetate and polyamide membranes have the commercially attractive combination of high rejection and water flux.

Microfiltration and ultrafiltration membranes are used for the separation and concentration of macromolecules and colloidal particles for sterile filtration and clarification. For instance, ultrafiltration has become the method of choice for protein concentration and buffer exchange. Recent work has also demonstrated the use of ultrafiltration for the purification of plasmid DNA and virus-like particles [13]. In this case, new composite regenerated cellulose membranes are used in these processes which can cause significantly less fouling, are more easily cleaned, have high mechanical strength and exhibit excellent permeability and retention characteristics. Enhanced mass-transfer modules, both rotating and Dean vortex systems, are also being developed for ultrafiltration applications. High-frequency back-pulsing has been used to improve process flux, reduce fouling and increase protein transmission in the purification of conjugated vaccine products.

Dialysis

Dialysis is a membrane separation process that allows the exchange of dissolved solute molecules in the feed for solvent molecules from a solution on the permeate side of the membrane [4]. The driving force for transport across the membrane in the case of dialysis is the difference in the chemical potential of the migrating species in the two phases separated by the membrane. This difference creates a gradient in chemical potential, which serves as a driving force for diffusion. For an ideal mixture, a gradient in chemical potential is equivalent to a gradient in concentration. Hemodialysis represents the largest membrane application in biomedical, replaces kidney function in three principal areas including removal of waste metabolites (urea, creatinine, endproduct of protein catabolism and metabolism), removal of excess body water, and restoration of acid-base and electrolyte balances. These solutes (up to 13K Dalton) accumulate slowly in end-stage renal disease (ESRD) patients and may have negative impacts on various metabolic regulatory mechanisms. Hemodialysis membranes have ultrafiltration capabilities ranging from 5 to 70 mL/h m^2 mmHg, with the minimum transmembrane pressure difference of 80 to 170 mmHg [3].

Electrodialysis

Electrodialysis is an electrically driven membrane separation process. Electrodialysis employs membranes that carry electrical charges in an arrangement that allows the concentration of ionic species [4]. Electrodialysis membranes, either anionic or cationic, are permeable to their respective ions when a direct-current voltage is applied [1]. This is created by the electrodes on each side of the cell. Separating the electrodes are several alternatively charged membranes; positively charged membranes are called anion exchange membranes, while negatively charged ones are known as cation exchange membranes. When the feed solution is introduced in between the charged membranes, the cations are driven to the cathode and the anions toward the anode. Cations can easily pass through the cation exchange membranes, but are repelled by the anion exchange membranes, which carry a net positive charge. The situation is reversed for the anions. The net result is a concentration of ionic species in alternative compartments and a corresponding depletion in the neighboring compartments. Electrodialysis depends on the unique charge-carrying membranes employed. Ion exchange membranes have been used for electrolysis of sodium chloride solution to manufacture sodium hydroxide and chlorine and desalting of protein solutions.

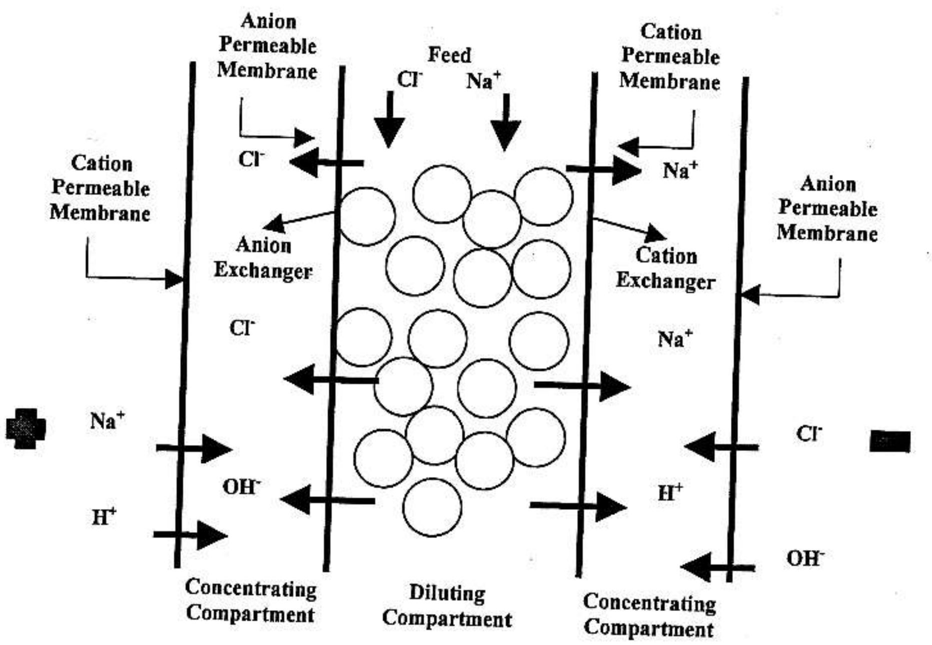

Figure 2: Electrodialysis Process

CURRENT STATUS AND FUTURE PROSPECTS OF MEMBRANE RESEARCH AND DEVELOPMENT (R & D) FOR BIOTECHNOLOGY IN MALAYSIA

Membranes have always been an integral part of biotechnology processes. Many industries involved in producing drinking water have now opted to membrane separation. A reverse osmosis system has been successfully installed in Sibu Island Resorts, Pulau Sibu Tengah, Mersing to produce water from seawater for the resorts' consumption [14]. Germanic technology which costs about RM100,000 is capable of producing 52,000 liter/day water [14]. According to a report in Singapore's *Straits Times*, Lyonnaise des Eaux and Transwater Corp had announced their joint bid for two water treatment contracts in Malaysia in 1997 valued at RM1 billion [15]. The contracts, each worth RM500 million, entail the purification of water for drinking in the states of Negeri Sembilan and Perak on the Western coasts of Peninsular Malaysia [15]. For many years, the Lyonnaise des Eaux Group has conducted research to get rid of tastes and smell in tap water. As a result, in 1996, Lyonnaise des Eaux Group has designed and developed a process known as Cristal (French acronym for combined reactors integrating liquid separation and adsorption). which combines an adsorption treatment on activated charcoal with a separation system using ultrafiltrating membranes [16]. Besides that, Dixy, Pink, Seamaster and Alpine have also currently joined the long line of membrane technology users in producing drinking water [17].

Furthermore, reverse osmosis, ultrafiltartion and microfiltration are the most commonly used membrane systems to treat industrial wastewater. Aquakimia Sdn. Bhd., Enersave Sdn. Bhd. and Motorola Malaysia Sdn. Bhd. use membrane units to treat their wastewater [17]. Equally important are the financial benefits that can accrue from waste recycling, product recovery and reuse. Water recycling upon treatment is another common practice one sees in many companies utilizing membrane units, where the wastewater is treated in order to recover the water before disposal. Some of the potential customers are treatment of cheese whey, metal finishing solutions, bleach and dye plant effluent, textile and pulp and paper industrial waste, and waste water from sewage treatment works.

Food and beverages industry in Malaysia has also been benefited by the presence of membrane technology, in which the typical applications include the treatment of cheese whey by ultrafiltration and removal of yeast from alcoholic beverages by microfiltration. In pharmaceutical sector, microfiltration is also used for the removal of microorganisms from the fermentation product such as to separate the microorganisms from the product antibiotics. In addition, membrane market in Malaysia has also been established for hemodialysis, in which B-Braun and Concords Medicals Sdn. Bhd. are among the active companies that involved directly in the development of this system [17]. The estimated market potential for medical industry is about RM75 millions, of which more than 67% is in hemodialysis [18].

As the membrane market is continue to grow in Malaysia, research and development of membrane technology is essential to enhance high-throughput and selectivity of membrane, to increase batch size coupled with projected reduction in production costs. Therefore, a closer working relationship or partnership between research institutions and the industry is required to improve membrane separation technologies. Latest advancement in membrane technology development by local establishment such as Membrane Research Unit (MRU) in University Teknologi Malaysia (UTM) is very encouraging and should be fully exploited by the industry, suppliers and entrepreneurs. The main activities of MRU include the production of high performance flat sheet and hollow fiber membranes, in which superselective hollow fiber membranes have been successfully developed by advanced spinning techniques. Besides that, defect-free and ultrathin-skinned asymmetric membranes have been produced by a newly-developed pneumatically-controlled flat sheet casting machine to increase membrane productivity and selectivity. In order to enhance the separation performance of recently available membranes, advanced membrane materials through polymer blending are adopted as well.

Furthermore, MRU is also involved in the development of membrane pilot-scale system, where membrane oxygen enrichment system for wastewater aeration has also been carried out to treat wastewater by biological digestion processes. The availability of hollow fiber membranes and membrane modules has brought forth the development of simple and economical reliable process for production of oxygen from ambient air. In addition, locally designed reverse osmosis and ultrafiltration systems for water purification is also one of the intensive research works. Hence, base on the continued efforts to develop improved membrane materials, modules, and process designs, membranes systems is expected to play an important role in the next generation of separation processes in Malaysia.

CONCLUSION

Nowadays, membranes are used in a variety of applications and have become an attractive system in biotechnology both in the world as well as in Malaysia. Membrane systems offer specific advantages in viable economics and flexibility, portability, compactness and mechanical reliability, simplicity in operation, energy-efficient and environmental-friendly. Currently, many membrane processes have been successfully applied in biotech industry. Indeed, membranes are among the various technologies that have perhaps the greatest prospects in future. Many new applications are likely to emerge in the coming years as the membrane properties continue to be improved and their unique advantages are adapted to the needs of various applications.

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