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# Application of Cell Membrane Principles in Molecular Separation Process with Membrane Technology on Food Science

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**Abstract.** The cell membrane is a feature in all types of human cells that functions as separator between inside and outside environment of the cell and composed of lipoprotein compounds. The function of cell membrane is to regulate entry and exit of substances from the cell through membrane transport system. There are two types of transport on membrane, passive and active transport. Membrane technology is inspired by the role of cell membranes. Membrane separation is a technique of separating mixture of 2 or more components selectively without using heat between two phases, homogeneous or heterogeneous and having different thicknesses. This review aims to determine the application of separation process with membrane technology in food sector and provide an overview, especially in membrane-based protein separation and purification technology. Membrane-based protein separation and purification technology uses membrane process with force of pressure, including microfiltration (MF), ultrafiltration (UF), nanofiltration (NF) and reverse osmosis (RO). Various applications of the separation process with membrane technology on food sector are protein separation at the processing of grain products (cereals), dairy products, beverage products, and animal products.

**Keywords:** cell membrane; food; membrane technology; molecular separation.

**Abbreviations**: MF = microfiltration; UF = ultrafiltration; NF = nanofiltration; RO = reverse osmosis

## INTRODUCTION

The cell membrane is a feature in all types of human cells that functions as separator between inside and outside environment of the cell. The cell membrane is composed of lipoprotein, a combination of lipids and protein compounds. These lipids and proteins have different properties, lipids are hydrophobic (insoluble in water) while proteins are hydrophilic (water soluble). The cell membrane has selective permeable properties that only certain molecules can pass. With this ability, cell membrane can limit activities that occur inside the cell and not easily affected by outside environment (Alberts et al., 2002).

One of the functions of cell membrane is to regulate entry and exit of substances from the cell. This function is carried out through membrane transport system. There are two types of transport on membrane, passive and active transport. Passive transport is molecular exchange process that occurs spontaneously and automatically without need special mechanism (does not require energy). Generally, passive transport occurs in molecules that can pass through the cell membrane at any time, for example water and glucose. The cause of passive transport in general is change in concentration gradient of these molecules (Meer, Voelker, & Feigenson, 2008).

Examples of passive transport are diffusion and osmosis. Diffusion is the movement of molecules from high concentration to low concentration area caused by kinetic energy of these molecules. The rate of diffusion depends on difference in concentration, molecular size, charge and solubility of molecules. Osmosis is the movement of water molecules through selectively permeable membrane from high concentration solvent (lots of water) to low concentration solvent (less water). The osmosis process will stop if concentration began in between two areas, where as osmosis occurs is in balanced state (Siegel, Agranoff, Albers, Fisher, & Uhler, 2009).

Active transport is the transfer of molecules through certain mechanisms that require energy. Active transport counters the nature of concentration gradient. Active transport requires the help of proteins which will act as transport molecules on membrane. Examples of active transport are sugar molecules and amino acids that are actively transported into cells using energy (Meer et al., 2008).

Membrane technology is inspired by the role of cell membranes. The membrane is attracting attention from various circles because of its very unique separation principle, transport and selective separation, also is more efficient than other operating units. The ability of membrane technology to separate components up to molecular level and is selective makes this technology usable in the separation process without involving chemical compounds so as to save operating costs. Membrane technology is also easy to enlarge or scale down due to its modular nature. Membrane technology has been widely used in biotechnology, such as the separation and purification processes of proteins. Membrane technology can be integrated with the reaction process so that products in form of proteins can be separated continuously from biological reactions (Nasori, 2016).

Membrane separation is technique for separating a mixture of 2 or more components without using heat. The membrane is selective barrier between two phases, either homogeneous or heterogeneous and have different thickness. The membrane functions to separate the material based on size and shape of molecule, hold components that have larger size than membrane pores and pass components that have smaller size. Filtration using membrane functioning as separation medium and also it functions as concentration and purification medium of solution that is passed through the membrane (Wenten, 2010).

Based on that, use of membrane technology which is an application of the working principle of cell membranes is important for separation process. So this review aims to determine the application of separation process with membrane technology in food sector and provide an overview, especially in membrane-based separation and protein purification technology.

## MATERIALS AND METHODS

### Procedures

This research was conducted using literature study method. The entire literature regarding cell membrane, membrane technology and molecule separation in food science was collected and studied. This is intended to obtain complete and scientifically proven information.

### Data analysis

The data obtained were analyzed in descriptive qualitative manner to determine the application of cell membrane principle to molecule separation on food.

## RESULTS AND DISCUSSION

### Membrane Technology Application on Protein Separation

The membrane is defined as a porous medium, in form of semipermeable thin film which functions to separate particles of molecular size in solution system. Larger molecule than membrane pore will be retained, while smaller molecule will pass through the membrane pore (Kesting, 2000). Separation process with membrane occurs due to differences in pore size, shape, and chemical structure. Semipermiable membranes can withstand certain molecule, but can pass others. The mixed phase to be separated is called feed, while the results of separation are referred to as permeate (Pratomo, 2003). In the membrane-based separation and purification process, it is necessary to attention for characteristics of material/material to be separated/purified and factors that can affect performance of the membrane such as molecular shape; membrane material used; and operational parameters which include pressure, temperature, concentration, pH, polarization and ionic strength (Wenten, 2010).

Membrane applications include protein separation and purification. Membrane technology allows protein separation easily and purified without going through methods/mechanisms that have been carried out, such as addition of additives or thermal conditions. The advantages of membrane technology are continuous separation; relatively low energy consumption; membrane processes are easily combined with other separations (hybrid processing); separation under adjustable operating conditions; easy to scale up; does not require additional ingredients; and easy to adapt because the material is adaptable. The disadvantages of membrane technology are flux and selectivity, because in the separation process using membranes, generally the phenomena that occur between flux and selectivity are inversely proportional (Nasori, 2016).

Membranes can be divided into porous and non-porous (dense) membranes. A porous membrane consists of membrane with a micro pore (microporous) and macro pore (macroporous). Whereas the non-porous membrane, there are no micro or macro-sized pores. The separation mechanism occurs through solute diffusion, where the separated components first dissolve in membrane, then diffuse through the membrane with help of driving force. Separation occurs due to differences in solubility. To obtain high permeability in non-porous membranes, the membrane structure is made as thin as possible and reinforced by layer thick to keep in the driving force in the form of pressure. This asymmetric membrane structure can separate molecules of the same size, either in liquid or gaseous form. Whereas in a porous membrane, the pore size determines separation characteristics. High selectivity can be obtained if the size of solute to be separated is larger than the pore size of membrane. The separation mechanism is in the form of a sieve that passes small (permeable) solutes and rejects large (non-permeable) solutes against the membrane pores with a driving force (Mulder, 2016).

Membranes can be classified based on material, thrust and pore size. One of the membrane technologies that are widely used in various fields are membranes with pressure-pushing forces, including microfiltration (MF), ultrafiltration (UF), nanofiltration (NF) and reverse osmosis (RO). MF and UF use porous membranes while NF and RO use non-porous membranes. The main factors for determining material separation in porous membranes are pore size and distribution as well as chemical and thermal stability of the membrane. Meanwhile, the non-porous membrane uses an asymmetric membrane. This membrane is used in gas separation/pervoration which is determined by the membrane performance, selectivity and flux (Hariyadi, 2005).

The MF membrane has a pore size between 100 nm - 10 μm and capable of being operated at pressure of 0.5 - 5 Bar. This membrane can be used to separate small particles such as microorganisms (cells, bacteria and viruses), while macromolecules (proteins, carbohydrates, fats), sugars, mineral salts and water pass through the membrane. The UF membrane has a pore size of 2 - 100 nm. UF membranes can be operated at pressure of 1 - 10 Bar. This membrane can separate all microorganism compounds, macromolecules, and sugars, but mineral salts and water can pass through the ultra-filtration membrane (UF). The nanofiltration membrane (NF) has a pore size of 1 - 2 nm. This membrane operates at pressure of 7 - 30 Bar and is used to separate all microorganisms, macromolecules, and sugars. Instead the mineral salts and still water passes through the membrane. Reverse osmosis (RO) has a pore size of 0.1 - 1 nm. This membrane is operated at pressure between 20 - 100 Bar. This membrane can be used to separate all microorganisms, macromolecules, sugars and mineral salts, but water passes through the membrane (Mulder, 2016).

MF is widely used for separation, purification and clarification of protein-containing solutions, such as separation and purification of extracellular proteins produced by fermentation, eliminating bacteria and viruses in therapeutic proteins. The basic operational concept of MF leads to a higher solute concentration which is closer to membrane surface than bulk feed flow. The effect of concentration polarization can be presented in MF applications because of the high flux and low mass transfer coefficient. This is due to the low diffusion coefficient of solutes in macromolecular and small particulate configurations, colloids and emulsions. The two standard modes used are dead end and cross flow operations. In cross flow mode, the liquid must be filtered by flowing parallel to the membrane surface and seeping through membrane due to pressure difference. The flow confluence reduces formation of material deposits and keep it at a low level in the filter (Trettin & Doshi, 1981).

In protein separation using UF, protein fractionation rapidly becomes more selective through enhancement of the membrane and module design. Compared to chromatographic methods, membrane separation techniques offer the advantages of lower costs and ease of scale-up for commercial production. However, the lack of membrane selectivity and fouling due to protein absorption during screening limits UF applications (Wakeman & Williams, 2002). UF membranes are based on various synthetic polymers, have high thermal stability, chemical resistivity, and limit the use of cleaning chemicals. Polyethersulfone (PES) is widely used as a material for UF membranes, due to its good thermal and stability properties and characteristics (Reis & Zydney, 2007).

**Applied of Membrane Technology in Food Science**

The application of membranes in food separation is carried out in the processing of grain products (cereals), dairy products, beverage products, and animal products. In grain product processing, membrane applications are used in the processing of soybeans and manufacture of corn starch. Soybeans are processed into processed products such as soy milk, tofu, yogurt, and cheese. Soybean processing produces protein which requires removal or reduction the content of several undesirable elements such as oligosaccharides, phytic acid and trypsin inhibitors. Conventional methods is used for protein separation by extraction, heat processing and centrifugation. This process is not optimal in obtaining products with desired properties. This process produces a semi-transparent liquid that remains during the deposition process with certain amount of protein. Another process developed to concentrate soy protein and isolates using the ultrafiltration membrane (UF) process with a hollow fiber configuration. The unwanted compound has smaller molar mass than pure protein and lipid concentration. The product from this membrane process has higher protein content than the product obtained by conventional processes. The purpose of using the UF/RO membrane is to hold as many low molecular weight proteins as possible in the permeate (Hariyadi, 2005).

The corn starch production process consists of several steps, including cleaning, soaking in hot water, coarse grinding, separation of institutions, separation of crude fiber and gluten from starch by centrifugation, purification and starch drying. The use of membranes in starch industry is quite potential, such as concentrating water from soaking corn using RO membranes, extraction and purification using MF, UF and NF membranes in order to obtain corn protein isolate, washing corn starch, concentrating and separating water on corn starch, starch hydrolyzate purification, concentration and water separation of corn starch, purification of corn starch hydrolyzate and purification of dextrose, fructose and glucose (McGregor, 2006).

The growth of microorganisms in milk can cause changes characteristics of milk, such as formation of acids, gases, mucus, changes in fat, taste, and aroma. To reduce the number of microorganisms in milk can be suppressed by sterilization/pasteurization process. The disadvantages of this conventional pasteurization process are damage to vitamin C in milk, protein denaturation, and damage to shelf life at low temperatures. The application of the microfiltration membrane (MF) or cold sterilization system in the dairy industry is important because it improves milk quality such as taste, storage time and protein content. Concentration polarization of milk often occurs in UF so that cross flow is used where direction of velocity is parallel to the membrane surface (Nasori, 2016).

Whey is a byproduct of milk processing industry which can affect the environment if it does not undergo proper handling. The membrane technology effectively separates components contained in whey such as fat, protein, salt and water. The membrane systems used are MF, UF and RO. The processing of whey protein peptides as functional and nutritional ingredients in the food, pharmaceutical and cosmetic industries has attracted attention over the years. Protein hydrolyzates should always be fractionated to obtain peptides with higher concentrations of functional and nutritional value. Since the differences in physico-chemical properties of these peptides are always small, separation techniques require differences in charge, size and hydrophobicity of the materials. Another potential technique is use of NF membrane so that the separation of solutes is based on charge and particle size of the solute (McGregor, 2006).

Coconut water is an isotonic drink with nutrients in the form of sugar 1.7 - 2.1%, protein 0.07 - 0.55% and mineral potassium. By using membrane technique, coconut water can be concentrated and used as a soft drink, fermentation medium, nata de coco production medium, and health drinks. MF membrane technology is not new technology for concentrating coconut water. MF membrane technology is operated by passing young coconut water through filter membrane made of polyacrylic polymer. The membrane is able to keep all microorganisms and particles in the form of sterile young coconut water permeate which has fresh aroma and taste (Meer et al., 2008).

Noni juice contains various active compounds, such as anthraquinones, terpentine, damnakantal, and seronin. Apart from active compounds, noni fruit also contains foul odor-producing acids, such as ascorbic acid, caproic, capric and caprylic. The process to produce this active substance is through the MF membrane, where the components that determine taste, color and aroma contained in fermented noni juice must be able to penetrate the membrane, while unwanted components such as the rest of the microorganisms will be retained by the membrane. To obtain certain active compounds, UF, NF and RO membranes can be used by first knowing the molecular weight of the active compound desired and pore size of the membrane (Wenten, 2010).

Seaweed can be processed to produce other high-value materials such as alginate, carrageenan, sorbitol and mannitol. Carrageenan is a type of polysaccharide that has molecular weight of 100,000 - 1,000,000 and is produced from the extraction of red seaweed. The carrageenan process is widely used in the manufacture of milk to increase viscosity of solutions and gels that can react with casein. The conventional process of carrageenan concentration is evaporation so that it requires a large amount of energy in the process (about 30 - 50 kWh/$m^3$ of water separated). The UF membrane is more effective technique to replace it. UF membrane materials that commonly used are polysulfone and polyamide. The advantages of UF membranes are the length of operation time can minimize use of chemicals, and energy requirements are much smaller (around 20 - 30 kWh/$m^3$ of water separated) (Nasori, 2016).

Gelatin is a compound commonly used in food industry because of its ability to form strong gel in solution medium. Gelatin is produced through selective hydrolysis of collagen (BM 100,000), which is an intracellular protein compound found in animal skin and bone tissue. Gelatin is obtained by extraction from the skin or bones with help of acids or enzymes. In the conventional process, an ion exchange apparatus is used to separate ions from the salt and is combined with an evaporation apparatus for concentration process. The membrane process has opportunity to replace this process. The advantage of UF membrane process is the module which able to pass salts as permeate and, then it simultaneously concentrating gelatin using small energy and economically advantageous. The flux produced from the polysulfone and polyethersulfone membranes was 10 - 60 L/$m^2$hour and 4 - 18 L/$m^2$hour respectively with a range of gelatin concentrations obtained, 3 - 20% (Mulder, 2016).

## CONCLUSIONS

Membrane-based protein separation and purification technology uses membrane process with force of pressure, including microfiltration (MF), ultrafiltration (UF), nanofiltration (NF) and reverse osmosis (RO). Various applications of separation process with membrane technology in food sector are protein separation in the processing of grain products (cereals), dairy products, beverage products, and animal products.

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