CHAPTER II
REVIEW OF RELATED LITERATURE

2.1 Chronic Renal Disease

Chronic kidney disease (CKD) is defined as kidney damage with or without decrease of glomerular filtration rate (GFR). It is diagnosed as such when GFR is less than 60 ml/min/1.73m^2 for a period of 3 months or more, irrespective of the cause. The high-risk population for CKD comprises elderly, obese, diabetic, and hypertensive individuals, including patients with auto-immune disorders or recognized urinary tract infections, and especially in diabetic nephropathy patients who evince a fast GFR decline. A decline in GFR produces electrolytic imbalances with adverse effects on the body's system, including fluid and hormonal changes, and eventually may be indicated as the cause of death [70, 71].

Mechanism of CKD progression: CKD is diagnosed based on the GFR and treatment to be considered is as presented in Table 2.1. The rate of CKD progression varies according to the underlying nephropathy and depending on the individual patient condition. Patients do not progress to ESRD in the early stages, but rather die prematurely of other causes, particularly cardiovascular events. Patient Stages 3 to 5 are often related to the progress to ESRD [72, 73]. In the last stage, RRT or transplantation has to be considered, because the GFR is usually less than 15 ml/min/1.73 m^2. ESRD is a devastating medical, social and economic problem; it consumes a vastly disproportionate amount of financial and human resources [74].

2.2 Renal Replacement Therapy (RRT)

End-stage renal disease (ESRD) refers to permanent damage to the kidneys that result in loss of normal kidney function (Ref). Patients' kidneys cannot get rid of the toxic waste and excess water. Patients with end-stage renal disease (ESRD) have a mortality rate 10–20 times that of the age-matched general population [75, 76].

Table 2.1: Classification of CKD and the clinical guideline evaluation [77]

Stage	GRF	Description	Clinical Action
1	>90	Kidney damage with normal or increase GFR	Slow progression, diagnosis and treatment,
2	60-89	Kidney damage with mild decrease GFR	Estimate the progression
3	30-59	Moderate decrease GRF	Treat the complications
4	15-29	Severe decrease GRF	Prepare for RRT
5	<15	Kidney failure	Start RRT (if uremia present)

The successful treatment outcome for ESRD patients can be managed by RRT such as hemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation (KT). Patients with end-stage renal disease (ESRD) are treated almost exclusively by HD and intermittent PD. Continuous ambulatory peritoneal dialysis (CAPD), or automated peritoneal dialysis, is a form of PD, and especially CAPD has been used worldwide over the last decades.

Peritoneal dialysis therapy was started in 1923; its first clinical application for the treatment of acute renal failure was carried out in and later successfully employed from 1946. It has been the most effective therapeutic option for ESRD patients since the late 1970s. CAPD is widely used to treat ESRD patients and has shown a dramatic rise in use worldwide, especially in developing countries [64, 78, 79].

In the standardization method intervention, 2L of dialysis solution containing 1.5 to 4.25 g/dL glucose is transfused continuously with 4-5 exchanges daily or intermittently into the peritoneal cavity through a permanently implanted catheter in the front abdominal wall [80, 81]. The process of CAPD intervention and how it eases a patient's lifestyle is presented in Fig. 2.1 below.

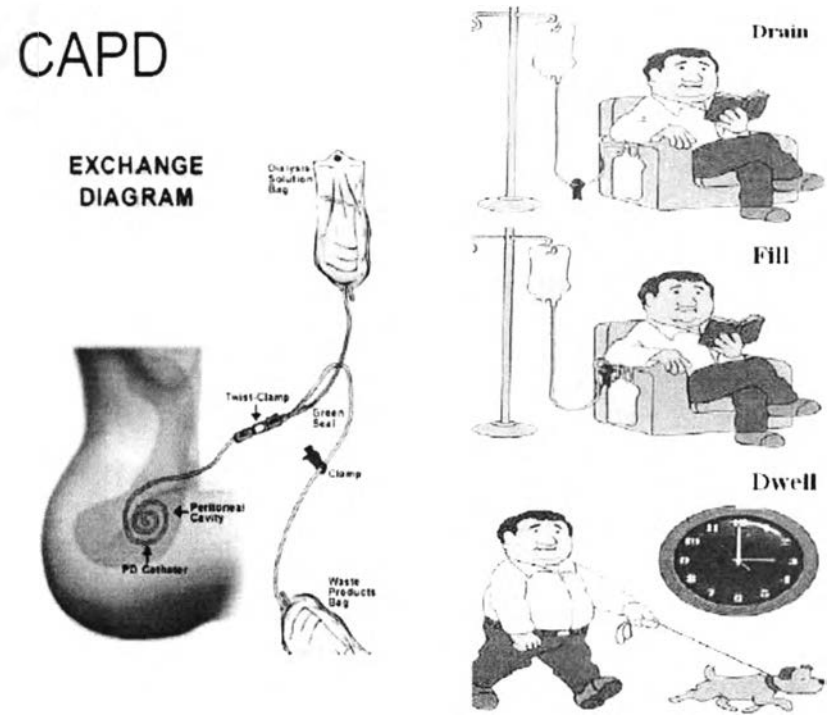

Figure 2.1: Overview of CAPD intervention

2.3 Peritoneal Membrane physiology

2.3.1 Peritoneal membrane anatomy:

In PD therapy, the peritoneal membrane is used as the dialyzing surface. The peritoneal cavity is the largest serosal cavity in the human body. The peritoneal membrane is a complex tissue. It consists of a single layer of mesothelial cells overlying an interstitial in which the blood and lymphatic vessels lie.

The mesothelial cells are covered by microvillia that markedly increase the surface area of 1-2m^2 in adults [82, 83]. There are two types of peritoneal membranes: the visceral membrane covering the abdominal organs, and the parietal peritoneum lining along the abdominal cavity. The visceral peritoneum begins in the posterior abdominal wall as a two-layer structure with the roots of mesentery, mesocolon, mesoappendix, and sigmoid mesocolon. The visceral peritoneum begins with the coronary ligament of the liver, the falciform ligament of the liver, and the gastrophrenic ligament attaching to the greater stomach curvature.

The liver lies intraperitoneally, covered by a single peritoneal layer. The stomach is covered with a single layer of the peritoneum. Along the greater stomach curvature, from the spleen to the duodenum, extends the greater omentum. The omentum is fused at the transverse colon, so that the omental bursa does not descend below the transverse colon into the greater cavity, as schematically in Fig. 2.2.

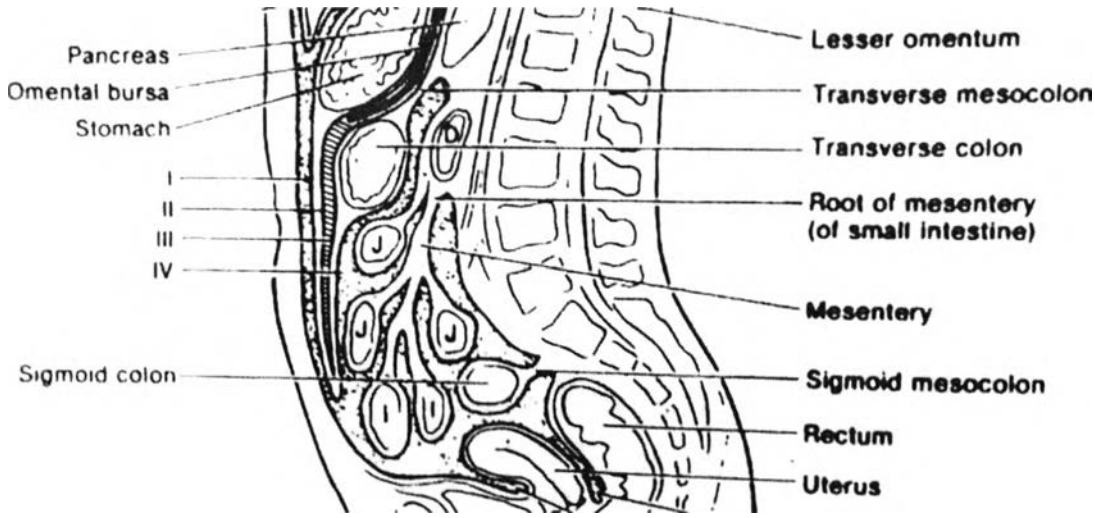

Figure 2.2: the peritoneal cavity anatomy. (Adapted from Zbylut J.)

The main parts of the peritoneal membrane comprise the cells, interstitium, connective tissue fibers, blood vessels and lymphatics. The total splanchnic blood flow in adult human is between 1000 and 2400 mL/min. This blood flows to the visceral organs, not to the small vessels of the peritoneum. Blood flow through the peritoneal capillaries probably does not exceed 200 mL/min. A high degree of capillarization can support a high blood flow, and the peritoneal membrane has endogenous capability to remove uremic toxins and water from body fluids of patients with ESRD during PD (80-82).

It has been reported that 10% of the total surface area is parietal; the other 90% is visceral omental or hepatic. Lymphatic drainage from the peritoneal cavity follows two major pathways: diaphragmatic and omental. The lymphatic vessels in the omentum also play a role in the removal of fluid from the peritoneal cavity [84-87]. The

mesothelium comprises flattened monolayer cells underlying a homogenous basement membrane. Mesothelial cells contain aqaporins, or water selective pores [88-90].

2.3.2 Function of the peritoneal membrane:

Healthy humans have minimal amounts of fluid in the peritoneal cavity. The principle function of the peritoneum is to provide contact between the intra-abdominal organs and the abdominal wall. The capillary endothelium constitutes a very selective barrier for solute diffusion [91, 92].

A two-pore model was described [93, 94]: The small pores are located within the inter-endothelial clefts. The large pores are represented either by channels of fused vesicles or by a few interendothelial gaps. Molecules larger than 4.2 nm in radius are excluded by the small pores and transported through the large pores. However, molecules pass through the large pores, comprising only 1/30,000 of the total number of pores.

Therefore, a 3-pore model was developed [95-98]: This model better conforms to experimental data. This indicates the existence of small paracellular pores (radius 47 angstrom), large pores (radius 250 angstrom) and ultra-small transcellular pores (radius 4-5 angstrom). The ultra-small pores are permeable to water but impermeable to almost all solutes and also have aquaporins localized in the peritoneal capillaries and mesothelial cells [99-103].

Moreover, the omentum is the first line of bacterial infection defense. The peritoneal cavity contains the immune cells macrophages and lymphocytes. The milky spots probably act as the responsiveness of immune defense mechanism. Macrophage form clusters near the peritoneal surface of the milky spots and are oriented toward the peritoneal cavity for migration [104, 105].

2.3.3 Peritoneal transport pathway: the fluid turnover in the peritoneal cavity is approximately 1L per day, constantly filtered from the capillaries and absorbed into the peritoneal cavity at the same rate[106]. The electrolyte absorption rate of infusion into the cavity depends on crystalloid and or colloid osmotic pressure [107, 108].

The capillary wall, the relative larger peritoneal interstitium and a few lymph vessels play an important role in bidirectional trans-peritoneal exchanges and macromolecules transportation between the blood and the peritoneal cavity. The process of solute and water transport during PD, the physiology and the local anatomy of the involved tissues are connected. However, there is no clinical data on the changes of the solute and water movement that occur in the tissue during clinical PD. Only the initial ultrafiltration and amounts of glucose, urea, creatinine absorbed were investigated. The pathway and direction of molecule exchange is illustrated in Fig. 2.3.

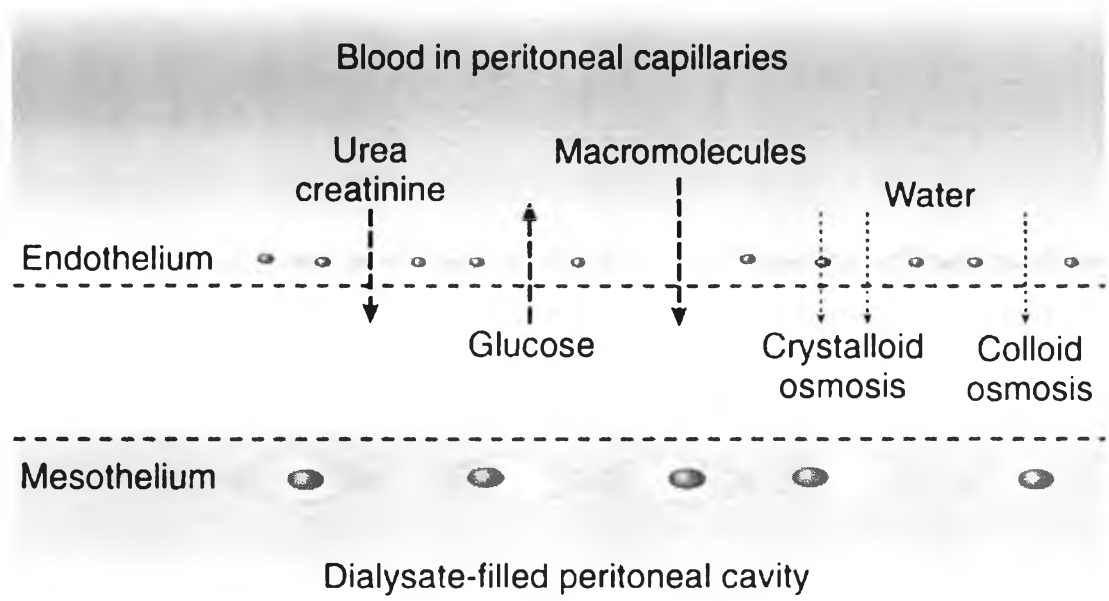

Figure 2.3: Pathways for solute and water transport (Adapted from Rippe *et al.*)

There are at least two different pathways to exchange across the capillary wall; first is the pathway by ultra-small pores (<0.5 nm) or aquaporins localized in the peritoneal capillaries and mesothelial cell for small solutes and water exchange; second is the paracellular pathway for fluid and small solutes up to albumin sized r=4.0-6.0 nm with an additional special large radius paracellular r>20 nm in the venular interendothelial gaps for macromolecules transportation. The ultrafiltration coefficient relates to small pores at approximately 85-90%, with 5-10% by the large pores [61, 109-113].

2.3.4 Peritoneal ultrafiltration

In osmotic ultrafiltration across the peritoneal membrane, glucose molecules in the dialysis solution generate the driving force for water removal from the peritoneal capillaries to the peritonea l cavity. This force occurs because of the difference between the concentration gradient between blood and dialysate, the molecular weight of the solute, and the peritoneal membrane resistance, which influence the rate of diffusive solute transport. If the concentration gradient maintains at greater than zero, solute removal will be continuous. However, clearance of urea cannot exceed a maximum of 40 mL/min unless with a more rapid exchanges of dialysis [56, 114, 115].

Regarding molecular size, smaller molecules diffuse more rapidly than larger ones, and the peritoneal membrane does not impede the passage of the solute up to the size of inulin (5200 daltons), while the larger solutes appears to be clearly restricted. The larger molecules create more oncotic pressure across the membrane, which acts in the same way as hydrostatic pressure, causing a bulk flow of water through the pores. That induces the convective flow, and the sodium and potassium are ultrafiltrates well below their respective concentration in the extracellular fluid, because of the sieving effect of the peritoneal membrane [109, 116].

Microcirculation: PD represents solutes and fluid exchange between the peritoneal capillary blood and dialysis solution in the peritoneal cavity across the peritoneal membrane [117]. Solute movement is mainly by diffusion based on the concentration gradient of the solute between dialysis solution and blood. It also moves across the peritoneal membrane by convection (the movement of solutes related to fluid removal) [118-123].

2.3.5 Peritoneal permeability:

The peritoneal membrane itself functions as a semi-permeable barrier regulating the selective transport of water and solutes between the systemic circulation and the peritoneal cavity during PD. The fluid movement, permeability or volume of ultrafiltration depends on the concentration of glucose in the PD solution, the length of time that the

fluid dwells in the peritoneal cavity, the number of exchanges per day and the individual patient's peritoneal membrane characteristics [119, 124, 125].

The permeability of the peritoneal membrane is used as the dialyzing surface in PD. The peritoneal membrane has negative charge; this makes negative charge solute such as phosphate move across the peritoneum more slowly than positive charge solute such as potassium. In any case, the mechanism of macromolecules such as albumin crossing the peritoneum is not completely understood, but is probably via lymphatics and through large pores in the capillary membranes.

2.4 Peritoneum characteristics and peritoneal dialysis

2.4.1 Peritoneal equilibration test (PET):

PET is a very important method used to examine ultrafiltration and clearance capability. It is also used to monitor peritoneal function characteristics [126, 127]. It is also used to evaluate the drain volume, to check how much dextrose is left in the fluid sample, and to check how much creatinine is found in the drained fluid and in the blood circulation. It is used to estimate peritoneum characteristics and can be graded as a high, average, or low transport rate by calculating the difference of glucose and creatinine levels in dialysate and in plasma. Characterization and interpretation are presented in Fig. 2.4.

How to evaluate peritoneal characteristics: the different solutes concentration during a dialysis exchange can be measured in the dialysate-to-plasma solute concentration ratio (D/P). In short, the method collects dialysate at 2 and 4 hours after PD infusion, with overnight drained dialysate was used as the control. Drained volumes were recorded and used to calculate the concentration. Blood samples at 2, 4 and 24 hour dwell times were collected. The collected dialysate and blood samples were tested for glucose and creatinine. The net ultrafiltration can be evaluated by calculating D/P of creatinine, D/D0 ratio (dialysate concentration/initial dialysate concentration) of glucose [128].

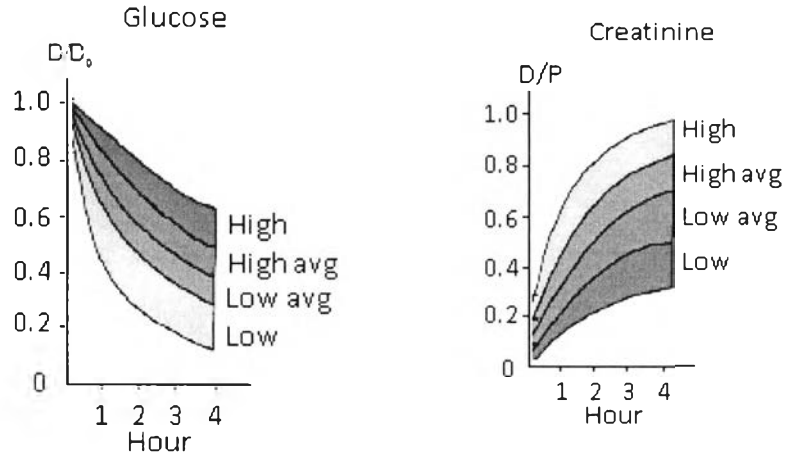

Figure 2.4: Interpretation of peritoneum equilibrium test

PET interpretation: a PD patient's peritoneal membrane can be categorized by the dialysate to plasma creatinine ratio (D/P) as high transport (>0.80), high average (0.65-0.81), low average (0.50-0.65), or low (<0.5) peritoneal transport capability, as presented in Fig. 2.4.

2.4.2 Peritoneal membrane changes

Knowledge of the peritoneal membrane transport type is important because it has been found that there is correlation between peritoneal membrane transport characteristic and mortality in peritoneal dialysis patients [129, 130]. It has been shown that an increasing peritoneal membrane solute transport rate matches an increasing mortality risk, as presented in Fig. 2.5.

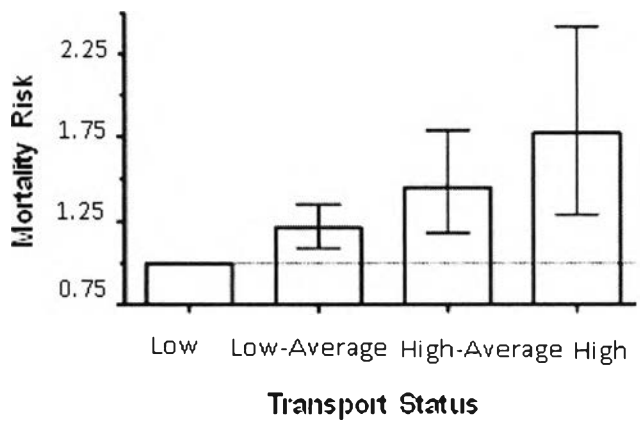

Figure 2.5: Pathways for solute and water transport

The peritoneal basement membrane plays a role in offering little resistance to solute diffusion. Layer thickness seems to affect solute transport. Patients on chronic peritoneal dialysis may develop a multi-layered basal lamina in post capillary venules and mesothelium of the parietal peritoneum. The submesothelial increased progressively in patients undergoing PD for a period of 2-4 years from 240 μm to 750 μm at 7-8 years compared to only 50 um in normal subjects. There are vascular changes associated with up-regulation of vascular endothelial growth factor (VEGF). It is widely believed that using conventional glucose-based PDF contributes to changes of both structure and function of dialyzing peritoneal membrane [131-133].

High transporter implies a structural or functional alteration of the peritoneum. There are both a larger effective peritoneal surface area and higher intrinsic membrane permeability of small solutes including creatine and urea. The vascularity increases in the membrane associate with an increased anatomic membrane area [129, 134] that induces an increase blood flow and increased effective small pore area in contact with dialysis solution, resulting in the loss of the osmotic gradient from the rapid absorption of glucose from the dialysate. Therefore, peritoneal membrane pore size is an important factor in the function of osmotic gent size and whether it can pass through either small or large pores [39, 96, 135].

2.5 Overview of peritoneal dialysis fluids (PDFs)

Peritoneal dialysis (PD) has been a well-established treatment for end-stage renal failure since the late 1970s [9, 46, 136-147]. This study focuses only on glucose-based PDF (GPDF) and corn derivative-based PDF (CPDF)[4, 43, 44, 148-151]. Glucose-based formulation is used as a standard PDF (Table 2.2). PD is an effective treatment for end-stage renal disease (ESRD) patients. One of the most important issues in PD therapy is how to reduce glucose exposure in order to avoid its metabolic side effects, including hyperglycemia, hyperinsulinemia, and obesity. Other difficulties include bioincompatibility, advanced glycated end-product generation, peritoneal damage, and, in the long-term, loss of ultrafiltration (UF) capacity. New alternatives to glucose as an osmotic agent were developed.

However, there are a number of disadvantages involved in this glucose-based solution, not only from the peritoneum exposure to high concentration of glucose, but also from degradation product effects, which can induce local peritoneal membrane toxicities leading to structure and function changes as well as many concerns of systemic biological effects that have eventually resulted in treatment failure [23, 150, 152]. Moreover, its rapid trans-peritoneal absorption contributed to a short duration of ultrafiltration. Over 15 years, glucose polymer corn derivative-based PDFs have been successfully introduced to overcome disadvantages and have provided more benefit to patients than those of glucose-based PDF [4, 11, 43, 153-155].It has shown a survival benefit, especially in glycemic control [156]. In addition, the use of glucose polymer-enhanced salt and water management and free water removal offers better extracellular water and total body water control as well as better sustaining of residual urine output [52, 157].

2.5.1 Conventional glucose-based PDF (GPDF)

A conventional dextrose base as osmotic agent in peritoneal dialysis fluid has been used for many years. However, long-term systemic exposure of glucose has been well recognized to cause a variety of adverse effects on the peritoneal membrane, in addition to other well-known systemic effects. PD solutions have a shelf life, and glucose over time degrades to form glucose degradation products (GDPs). Several studies [42, 67, 151, 158-160] in both in vivo and in vitro have shown that conventional solutions damage mesothelial cells lining the peritoneum, cause peritoneal membrane thickening, and lead to changes of peritoneal blood vessels [35]. Dextrose-based solutions have been shown to cause structural as well as functional changes in the peritoneal membrane, which in long-term patients ultimately leads to ultrafiltration failure and discontinuation of PD [161-163].

A conventional glucose-based PDF contains unphysiological compositions such as acidic pH, high concentration of glucose and GDPs and contribution of AGEs (see Table 1.1 & 1.2). The glucose concentration is 15-40 times the physiological level [31] (within the range of 1500 to 4250 mg/dL). After intraperitoneal equilibration, the glucose

concentration remains at 6–16 times that of the physiologic concentration. The long-term exposure to high glucose levels induces serious adverse metabolic effects on peritoneal tissue. Moreover, high glucose solution contains GDP which is well known to cause cytotoxicity [35, 151, 164-166].

Recent research reports that GDPs inhibits cell proliferation, induces apoptosis, and influences fibrosis, thickening of the peritoneal membrane and peritoneal transport characteristics in animal studies [57, 131, 167]. Moreover, GDP impairs mesothelial cell function and modulates generation of various cytokines, including of IL-6, TGF-beta and VEGF [164, 165, 168-171].

Long-term exposure to GDPs in PDF results in progressive deterioration of the mesothelial cell layer, fibrosis and others factors and contributes to ultrafiltration failure. The 3, 4-dideoxyglucosone-3-ene (3, 4-DGE) is the main molecule of GDPs that can cause acute cytotoxicity and is the most bioreactive of all GDPs; therefore it has become the marker for evaluating biocompatibility of PDFs. Its bio-incompatible components induce development of peritoneal fibrotic changes in long-term PD patients [152, 172-174]. A patient peritoneal shows morphological changes, fibrosis and finally dysfunction [36, 175, 176]. The encapsulating peritoneal sclerosis is a serious complication of PD therapy. Thus, avoidance of these problems and prevention of peritoneal side effects are important considerations in PD therapy [18, 58, 131, 165, 177].

Glucose in high concentrations is shown to be toxic for the mesothelium *in vitro* and animal studies [178, 179]. Peritoneal pathogenetic changes could be induced by daily peritoneal exposure to a 3.86% GPDF in human and rats [49, 180]

Besides the metabolic disturbances as shown above, glucose-based PDF showed several disadvantages: it induces rapid absorption across the peritoneal membrane and leads to desperation of the osmotic gradients. Ultrafiltration is low, particularly in patients with fast peritoneal membrane transport. Moreover, long-term exposure to high glucose concentration contributes to progressive membrane alteration (Table 2.2) that finally may lead to UF capacity failure (Fig. 1.2).

2.5.2 Corn derivative-based PDF (CPDF)

To reduce incompatibility of the solution, many attempts at locating alternative solutions have been evident over the recent decade [45, 49, 181-188]. One promising attempt has been the introduction of a glucose polymer, corn-based glucose polymer (CPDF) with the trade name CPDF, which has been used as PD over the past 17 years [45, 153, 154, 160, 189-201]. It is composed of 7.5 corn-based glucose polymer (g/L) and electrolytes sodium 132 chloride 96, calcium 3.5, magnesium 0.5 and Lactate 40 (mEq/L); the osmolarity 282 (mOsm/kg) and pH 5.2-5.6 [40].

Cornstarch-based glucose polymer is a water-soluble glucose polymer isolated by fractionation of hydrolyzed cornstarch. It has an average molecular weight (MW) of 16,800 Da ranges from 13000 to 19000 Daltons and has a MW distribution of which 85% of the molecules vary from 1638 (approximately ten glucose units) to 45000 Daltons (approximately 2-300 glucose units). The mixture has an average high MW (HMW) of 16200 Da and less than 6% has a lower MW (LMW) of 1638 Da. The linking of glucose molecules are predominantly by alpha-(1–4) glucosidic bond (amylose) more than 90% with a small proportion of branched chains linked by alpha-(1–6) (amylopectin) less than 10% as presented in Fig. 2.6. [38, 39, 202, 203].

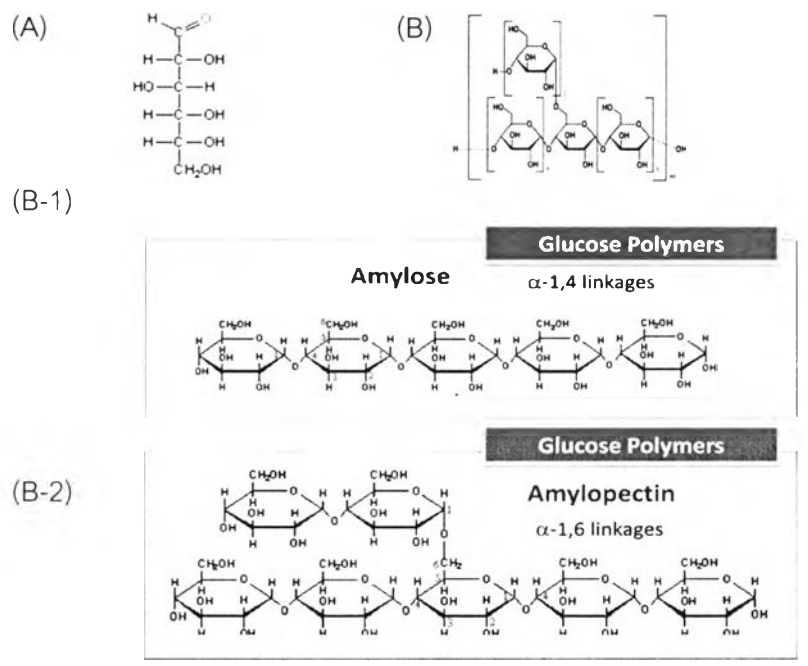

Figure 2.6: Molecular chemical structures of glucose and glucose polymer.

Glucose (A), starch (B) and its different form of glycosidic bonding: amylose with α-1,4 linkages (B-1) and amylopectrin with α-1,4 linkages (B-2).

CPDF is iso-osmolar to serum (282 mOsm/kg) with physiologic pH, biocompatible buffered. The patient requires only one bag per day (long dwell). Its positive ultrafiltration is sustained for over 12 hours. Many clinical studies have shown that 7.5% corn-based glucose polymer gives a prolonged net ultrafiltration in a PD patient equivalent to 3.86% glucose-based during a long dwell. It functions as a colloid osmotic agent to achieve ultrafiltration during long (12-16 hours) PD dwells. A mixture of poly-disperse glucose polymer provided superior satisfaction of net ultrafiltration performance with a slow rate of absorption closely related to an average MW by a mechanism resembling "colloid" osmosis [38]. The amount of ultrafiltration (UF) achieved by the conventional GPDF depends largely on the concentration of glucose used (1.5%, 2.5%, or 4.25 anhydrous glucose). The higher the concentration, the higher the UF volume obtained (Fig. 2.7).

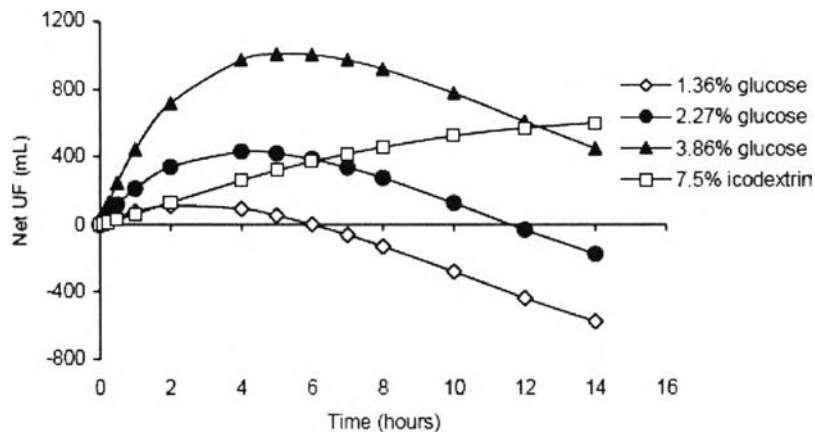

Figure 2.7: Compare net ultrafiltration between 7.5% corn derivative-based PDF and 1.5%, 2.5%, 4.25% dextrose [56, 204].

Glucose or other small molecules are absorbed from the peritoneal cavity primarily by diffusion across the peritoneal capillary endothelium, but the diffusion is limited for a large molecule of glucose polymer. Glucose polymer with its high molecular weight absorption occurs primarily via the relative slow convective fluid movement out of the peritoneal cavity by a colloidal properties, rather than crystalline osmotic pressure. It

acts in the peritoneal cavity by exerting osmotic pressure across small intercellular pores resulting in transcapillary ultrafiltration through the dwell. This is due to the fact that the polymer is minimally absorbed across the peritoneal membrane.

As a result, the absorption of colloid osmotic agent is much slower than crystalloid small molecules (Fig. 2.7). Only 20%-40% of the administration CPDF is absorbed from the peritoneal cavity during a 12 hour dwell. Therefore, glucose polymer creates a longer-lasting osmotic pressure, resulting in a longer duration of osmotic gradient which will decline only slowly, but sustains a positive net UF throughout a long dwell [4, 56, 205].

Movement of the polymer derivative from dialysate-to-plasma is dependent on fraction size. HMW fractions are cleared by lymphatic convection and small LMW fractions diffuse into the peritoneal tissues and then to the blood space via the capillaries. There are significant increases in dialysate concentrations of low molecular weight, DP2-DP7, fractions by the end of 12-hours [39, 202]. The appearance of oligosaccharides as a consequence of hydrolysis of larger MW fractions is observed, with no evidence of long-term accumulation and return to baseline upon discontinuation of use [202].

Table 2.2: Effect of PDFs on peritoneal membrane function [165, 170, 171, 206-208]

	Glucose[a]	Corn-based glucose polymer[b]
***In vivo* effects**		
Mesothelium	Denudation	Preserved
Submesothelium	Thickening	↓ Thickening
Vascular changes	Vasculopathy	↓ Angiogenesis
AGE deposition	Increased	Decreased
***Ex vivo* effects**		
IL-6 secretion	Decreased	Increased
TGF-β1 secretion	Increased	Increased
***In vitro* effects**		
Cell proliferation	Inhibition	Improved

Cell viability	Decreased	Improved
Mitochondril damage	Increased	Improved
IL-6 secretion	Decreased	Increased
TGF-β1 secretion	Increased	No change
VEGF secretion	Increased	?
Collagen I synthesis	Increased	Decreased
Collagen III synthesis	Increased	Increased
Collagen IV synthesis	Increased	Decreased

[a] compared to control, [b] compared to glucose-based fluids

CPDF has physiologic pH, biocompatible buffered. The different properties of polydisperse polymers decided the different ability of the glucose polymer-based PDF for volume expansion and difference of osmotic effectiveness [39]. Researchers found an independent significant association between improved survival and at least 6 months' use of CPDF compared to non-users. There is a significant association between improved survival and glucose polymer CPDF users [1, 138].

Although CPDF is safe and offers several advantages [1, 56, 138, 206, 208], however, the cost of the solution is relatively high [209]. In addition, it is a possible cause of cutaneous hypersensitivity reaction. There was about 10.1% higher incidence of rash compared with glucose regimes and some adverse effect was reported [62, 210, 211]. In most reports, rash occurred early, within 3 weeks of CPDF initiation, which involved palms and soles. The pathophysiology of cutaneous hypersensitivity to CPDF is still unknown. The polymers differ in their linkage of glucose molecules, α- 1, 4 for CPDF and α-1, 6 for dextran.

There is some disadvantage information reported. Erythematous, itchy, maculopapular rash over the trunk and the back had been found in a 50-year-old prescription woman on continuous cyclic peritoneal dialysis (PD) with glucose exchanges with an add-on last filling of 7.5% corn derivative-based PDF. A similar presentation was also seen in another woman who came with a similar presentation of rash; although seven weeks after 7.5% corn derivative-based PDF initiation and who

also responded to stoppage of 7.5% corn derivative-based PDF. These patients had used same lot number of 7.5% corn derivative-based PDF supplies.

New alternative TPDF development

Although corn-based glucose polymer yields many advantages, there are reports that CAPD patients using this solution had adverse effect reactions as above described. Importantly, the corn-based glucose polymer solution was manufactured by a monopoly company and had to be imported, so the cost of usage is high.

To avoid a negative balance of Thai import-export and to reduce disadvantages of corn-based glucose polymer-containing solutions, our research team has developed a branched glucose polymer called "tapioca-based glucose polymer" from a taioca starch, since we know that tapioca is one of the major starch products of the Thai agricultural economy. A modified tapioca derivertive may potentially be produced in Thailand.

Tapioca-based PD is a hydrolyzed fraction of dextrin (glucose polymer) isolated from tapioca starch. The polymer of glucose has an average MW of 11,000 Dalton. The structure of a tapioca derivative is similar to a corn starch derivative-based PDF. Its structure is based on polysaccharide polymers of D-glucopyranose linked by approximately 7-8% α-1, 6 glucosidic linkages and more than 90% α-1, 4 glucosidic bonds.

This better bonding might possibly make its structure with more stable. A stable structure may slow metabolites and improve peritoneal ultrafiltration. Therefore the underlying effects and mechanism of a tapioca-based glucose polymer in terms of safety and effectiveness need to be examined.

TPDF is a novel PD solution containing the glucose polymer, and this solution may well offer an improvement to the peritoneal environment compared to glucose-based and corn-based solutions as well as improvement of ultrafiltration and clearance. Therefore, in this study, we have aimed to investigate the efficacy of the newly-developed PD solution "tapioca-based glucose polymer" in terms of safety and effectiveness.