**Separation Mechanism**

Phenols, obtained by PhenolSep SP in front fractionate into large and small molecules for weight components by Cascadeflo® EC, using column separation components including performance substances each of PS2 and CILP are dissolved. Small molecules weight components including valuable substances such as albumin are returned to the patient.

**Specifications**

- **EC-30W**
  - fiber filter material: Cellulose ester and cellulose polymer
  - internal diameter: 17.5mm
  - surface area: 4.5m²
  - maximum flow rate: 1.5L/min
  - maximum volume: 160L
- **EC-50W**
  - fiber filter material: Polypropylene
  - internal diameter: 17.5mm
  - surface area: 4.5m²
  - maximum flow rate: 1.5L/min
  - maximum volume: 160L

**Use of EC-30W**

Use of EC-30W is needed for the removal of residual 5% or less of albumin and 7% or less of Hb can be removed using EC-30W with a smaller internal diameter. The capacity of the filter is about 50% lower than that of EC-50W, and it requires a higher rate of fluid flow. EC-30W is used for subjects with severe hypotension or when the patient's condition is unstable.

**Use of EC-50W**

EC-50W is also used for the treatment of patients with severe hypotension, and it is recommended for the treatment of patients with chronic kidney disease. EC-50W is used for patients with severe hypotension or when the patient's condition is unstable.

**References**


**AsahiKASEI MEDICAL CO., LTD.**

A Partner in Blood Purification
Cascadeflo EC Size: W625mm X H297mm

Indication
The Cascadeflo EC is designed for use in double filtration phosphorus (DFP) to fractionate the plasma separated by the plasma separator into large-molecular plasma and small-molecule plasma.

Features of Cascadeflo EC
- Highly selective filtration of small molecule
- Minimal risk of patients' own peculiar non-pathological substances, e.g., albumin
- No risk of infection from replacement fluid
- Reduces protein leakage to replace the fluid

Sharp Cut-off Curve
Haemofiltration separation of plasma side provides sharp cut-off feature

a) Permeability

b) Cut-off Curve

Stable Sieving Coefficient
Unique membrane performance of low filter results in stable sieving and enables stable plasma performance

Clinical Experiences of DFP

- **Metabolic Disorders**
  - Focalized hyperparathyroidism (PH)
    - LDL spectrum is applied for PH patients who have either ineffective or not tolerated maximum medication therapy and ineffective dialysis therapy. LDL cholestrol (LDL-C) can be removed from plasma by adsorption precipitation, or filtration devices or from whole blood. ALCOR, adsorption methods are effective in reducing LDL-C levels (LDL-C). A study compared three times of LDL-C column (ITA-1A, AVE-2500) with respect to side effects (S) in three cases with PH who went through six treatments with each of the administration methods. LDL-C column was adopted after blood with LDL-C (AVE-2500) after plasma therapies.
  - LdlA hyperproteinaemia
    - LdlA is a circulating lipoprotein that resembles LDL-C, increasing levels of LdlA increase in risk of myocardial infarction (MI). Beneficial effect of LdlA therapies in the incidence of major adverse coronary events (MACE) was observed in the retrospective study (LA). Incidence of MACE in 10 patients who had received LDL-C was evaluated for two years before and after commencement of LDL-A therapy. Ldla was observed. Incidence of MACE was significantly decreased from 30% in the last year of follow-up to 5% in the first year of DFP (AIC). LA

- **Organ Transplanat**
  - HLA-ABO-incompatible kidney transplant
  - DFP is an established modality of anti-HLA antibodies and anti-blood group removal in ABO-incompatible and ABO-mismatched kidney transplants. Antibody-mediated rejection (AMR) is an important cause of acute and chronic allograft dysfunction and graft loss. Desensitization protocol including therapy and retransplantation before transplant was performed in 30 cases with HLA-ABO-incompatible major kidney transplant. The incidence of AMR was significantly decreased in DFP cases with previous desensitization who did not receive desensitization. The graft survival rate was improved to compatible cases.

- **Renal Diseases**
  - Systemic lupus erythematosus (SLE)
    - DFP is effective for eliminating pathogenic molecules such as anti-DNA antibody and immune complexes in SLE patients. Clinical benefit of patients (SLE) or immunoadsorption was evaluated in lupus nephrotic (LN) patients in three groups. Intravenous cyclophosphamide pulse therapy (IVCy) group (16 cases), production of sparsely of ANC and Evac group (15 cases). The incidence of remission was compared in proximal and R/CY groups. Combining therapy group had higher complete remission rate. Combination therapy may be expected after achieving the complete remission of LN, and in preventing the renal relapse and progression. DFP is applied after a certain cycle of DFP, showing an evident improvement of anti-DNA antibody and LN activity.

- **Dermatologic Disorders**
  - Periphervitis
    - Periphervitis is an autoimmune skin inflammining disease in which dermograph, an epidermal cell adhesion molecule is stained by autoantibodies. Periphervitis is an autoimmune skin inflammining disease caused by extracellular cell adhesion and antibody. Mediation of periphervitis involves the administration of corticosteroids, immunosuppressors and DFP, DFP is applied for patients who is resistant to medication or patients suffering from complications of medication. In cases of periphervitis in 3 cases in pancreas in 3 cases in periphervitis in 1 received series of DFP, resulted in an improvement in clinical symptoms and remission.

Examples of Applications
- Based on Japanese health insurance coverage and references 1 to 17
- **Organ Transplant**
  - HLA-ABO-incompatible kidney transplant
    - DFP is an established modality of anti-HLA antibodies and anti-blood group removal in ABO-incompatible and ABO-mismatched kidney transplants. Antibody-mediated rejection (AMR) is an important cause of acute and chronic allograft dysfunction and graft loss. Desensitization protocol including therapy and retransplantation before transplant was performed in 30 cases with HLA-ABO-incompatible major kidney transplant. The incidence of AMR was significantly decreased in DFP cases with previous desensitization who did not receive desensitization. The graft survival rate was improved to compatible cases.

- **Rheumatic Disorders**
  - Systemic lupus erythematosus (SLE)
    - DFP is effective for eliminating pathogenic molecules such as anti-DNA antibody and immune complexes in SLE patients. Clinical benefit of patients (SLE) or immunoadsorption was evaluated in lupus nephrotic (LN) patients in three groups. Intravenous cyclophosphamide pulse therapy (IVCy) group (16 cases), production of sparsely of ANC and Evac group (15 cases). The incidence of remission was compared in proximal and R/CY groups. Combining therapy group had higher complete remission rate. Combination therapy may be expected after achieving the complete remission of LN, and in preventing the renal relapse and progression. DFP is applied after a certain cycle of DFP, showing an evident improvement of anti-DNA antibody and LN activity.

- **Dermatologic Disorders**
  - Periphervitis
    - Periphervitis is an autoimmune skin inflammining disease in which dermograph, an epidermal cell adhesion molecule is stained by autoantibodies. Periphervitis is an autoimmune skin inflammining disease caused by extracellular cell adhesion and antibody. Mediation of periphervitis involves the administration of corticosteroids, immunosuppressors and DFP, DFP is applied for patients who is resistant to medication or patients suffering from complications of medication. In cases of periphervitis in 3 cases in pancreas in 3 cases in periphervitis in 1 received series of DFP, resulted in an improvement in clinical symptoms and remission.

- Organ Transplant
  - HLA-ABO-incompatible kidney transplant
    - DFP is an established modality of anti-HLA antibodies and anti-blood group removal in ABO-incompatible and ABO-mismatched kidney transplants. Antibody-mediated rejection (AMR) is an important cause of acute and chronic allograft dysfunction and graft loss. Desensitization protocol including therapy and retransplantation before transplant was performed in 30 cases with HLA-ABO-incompatible major kidney transplant. The incidence of AMR was significantly decreased in DFP cases with previous desensitization who did not receive desensitization. The graft survival rate was improved to compatible cases.

- Neurological Disorders
  - Cerebral palsy (CP)
    - DFP is effective for eliminating pathogenic molecules such as anti-DNA antibody and immune complexes in SLE patients. Clinical benefit of patients (SLE) or immunoadsorption was evaluated in lupus nephrotic (LN) patients in three groups. Intravenous cyclophosphamide pulse therapy (IVCy) group (16 cases), production of sparsely of ANC and Evac group (15 cases). The incidence of remission was compared in proximal and R/CY groups. Combining therapy group had higher complete remission rate. Combination therapy may be expected after achieving the complete remission of LN, and in preventing the renal relapse and progression. DFP is applied after a certain cycle of DFP, showing an evident improvement of anti-DNA antibody and LN activity.

- Dermatologic Disorders
  - Macular dystrophy (MD)
    - DFP is effective for eliminating pathogenic molecules such as anti-DNA antibody and immune complexes in SLE patients. Clinical benefit of patients (SLE) or immunoadsorption was evaluated in lupus nephrotic (LN) patients in three groups. Intravenous cyclophosphamide pulse therapy (IVCy) group (16 cases), production of sparsely of ANC and Evac group (15 cases). The incidence of remission was compared in proximal and R/CY groups. Combining therapy group had higher complete remission rate. Combination therapy may be expected after achieving the complete remission of LN, and in preventing the renal relapse and progression. DFP is applied after a certain cycle of DFP, showing an evident improvement of anti-DNA antibody and LN activity.

- Others
  - Peripheral arterial disease (PAD)
    - DFP is effective for eliminating pathogenic molecules such as anti-DNA antibody and immune complexes in SLE patients. Clinical benefit of patients (SLE) or immunoadsorption was evaluated in lupus nephrotic (LN) patients in three groups. Intravenous cyclophosphamide pulse therapy (IVCy) group (16 cases), production of sparsely of ANC and Evac group (15 cases). The incidence of remission was compared in proximal and R/CY groups. Combining therapy group had higher complete remission rate. Combination therapy may be expected after achieving the complete remission of LN, and in preventing the renal relapse and progression. DFP is applied after a certain cycle of DFP, showing an evident improvement of anti-DNA antibody and LN activity.

- **Gastroenterologic Disorders**
  - Hypertensive disease (HD)
    - DFP is effective for eliminating pathogenic molecules such as anti-DNA antibody and immune complexes in SLE patients. Clinical benefit of patients (SLE) or immunoadsorption was evaluated in lupus nephrotic (LN) patients in three groups. Intravenous cyclophosphamide pulse therapy (IVCy) group (16 cases), production of sparsely of ANC and Evac group (15 cases). The incidence of remission was compared in proximal and R/CY groups. Combining therapy group had higher complete remission rate. Combination therapy may be expected after achieving the complete remission of LN, and in preventing the renal relapse and progression. DFP is applied after a certain cycle of DFP, showing an evident improvement of anti-DNA antibody and LN activity.
Cascadeflo EC
Size: W625mm X H297mm

Indication
The Cascadeflo EC is designed for use in double filtration pheresis (DFPP) to fractionate the plasma separated by the plasma separator into large-molecule plasma and small-molecule plasma.

Features of Cascadeflo EC
- Non-suction collection of anticoagulant fluid
- Minimal load on patients against nonsurgical antithrombotic substances, e.g., heparin
- No or minimal risk of injection site reaction
- Reduced risk of coagulation in the blood bag
- Features possible proton leakage to replacement fluid

Sharp Cut-off Curve
Homogeneous distribution of pore size provides sharp cut-off feature

- a) Permeability
- b) Cut-off Curve

Stable Sieving Coefficient discus performance of membrane units

Circuit Diagram

Clinical Experiences of DFPP

- Metabolic Disorders
  - Focal hyperlipoproteinemia (FH)
  - LDL apheresis is applied for patients who have either ineffective or intolerable maximum medication therapy and ineffective dialysis. UR, cholesterol, and other plasma lipids can be removed from patients by adsorption, precipitation, or filtration devices or from whole blood. LDL apheresis methods are effective in reducing LDL levels (LDL)
  - A study compared three techniques of dialysis treatment. LDL apheresis was associated with a significant reduction in LDL-C levels compared with standard dialysis and compared favorably with LDL apheresis.

- Late hyperprolactinemia
  - Late hyperprolactinemia is associated with increased levels of prolactin release of lactogenic inhibition (LH). The effect of LN apheresis in the incidence of major adverse coronary events (MACE) was observed in the retrospective study (LH). Incidence of MACE in patients who have received LN apheresis was evaluated for two years before and after commencement of LN apheresis. The prospective observational multicenter study (LH) cases with MACE were enrolled. Incidences of MACE were significantly decreased from 20% in the non-hyperprolactinemia group to 15% in the hyperprolactinemia group.

- Organ Transplantation
  - HLA-A260-incompatible kidney transplant
  - DFPP is an established modality of anti-LA and anti-DL antibodies in HLA-compatible and A260-incompatible kidney transplant. Anti-LA metabolite receptor (AMR) is an important cause of acute and chronic allograft dysfunction and glomerulosclerosis. Desensitization protocol including therapy and immunosuppression before transplant was performed in 30 cases. AMR was significantly lower than in non-desensitization group.

- Rheumatologic Disorders
  - Systemic lupus erythematosus (SLE)
  - DFPP is effective for eliminating pathogenic molecules such as anti-DNA antibody and immune complexes in SLE patients. Clinically relevant of SLE (SLE) was evaluated in lupus nephritis (LN) patients in three groups, i.e., plasma apheresis group (PAG), immunosuppressive pulsed therapy (IPT) group, and combined treatment group (CTG). Combined treatment rate was comparable in plasma apheresis and CTG groups, while combination group had higher complete remission rates.

- Dermatologic Disorders
  - Periphyperegia
  - Periphyperegia is an autoimmune skin blistering disease in which desmoglein, an epidermal cadherin molecule is targeted by antibodies. Periphyperegia is an autoimmune skin blistering disease caused by extracellular matrix proteins. Immunoblockage with DFPP is applied for patients who are resistant to medication or patients suffering from complications of medication. In cases in periphyperegia and cases in pemphigus foliaceus ( PF), the efficacy of DFPP was demonstrated.

- Gastrointestinal Disorders
  - Peritoneal dialysis
  - Peritoneal dialysis is a form of dialysis in which the abdomen is used as the dialyzer. DFPP is an effective technique for patients suffering from complications of medication or patients suffering from complications of medication in cases of patients with PF and cases in pemphigus foliaceus. DFPP is also effective in improving clinical symptoms and remission.

Examples of Applications
- Peritoneal dialysis (PDT)
  - By eliminating (D)I particles and high molecular weight proteins, DFPP decreases peritoneal transit and thereby improves homeostasis in macrophage (M). In 2 cases suffering from PF and cases, three cases experienced complete remission of ulcers and the other two cases had a partial remission of ulcers after a cycle of DFPP sessions. Without reducing any adverse effects (2), it cases with non-healing fistula ulcers caused by severe ischemic diabetic foot syndrome underwent DFPP sessions, fistula healing was accelerated in four cases and was unchanged in 3 cases, but with an increase in IPD that allowed successful minor amputation (3).

- Gastrointestinal Disorders
  - Peritoneal dialysis (PDT)

- Rheumatologic Disorders
  - Systemic lupus erythematosus (SLE)

- Dermatologic Disorders
  - Periphyperegia

- Gastrointestinal Disorders
  - Peritoneal dialysis (PDT)

- Others
  - Peritoneal dialysis (PDT)

- Recommended model
  - FCD-300, 2000
  - FCD-400
  - FCD-400
  - FCD-400

- Others
  - Peritoneal dialysis (PDT)
**Cascadeflo EC**
Size: W625mm X H297mm

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**Features of Cascadeflo EC**
- **Wide applicability by selection of optimal mode**
- **Minimal risk to patients even beside no-pathological substance, e.g., albumin**
- No or minimal risk of infection from replacement fluid
- **Possible protein allergy to replacement fluid**

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**Sharp Cut-off Curve**

Hemocompatibility evaluation of pore side provides sharp cut-off feature

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**Clinical Experiences of DFPP**

- **Metabolic Disorders**
  - **Familial hypercholesterolemia (FH)**
    - LDL-apoE is applied for patients who have either ineffective or no tolerated maximum medication therapy and ineffective dialysis. LUS-chelation therapy can be removed from patients by absorption precipitation, or filtration devices or from whole blood. LUS-apoE methods are effective in reducing LDL (VLDL) levels (1). A study compared three cases of LDL apoE columns (7-7, LA-7, LF-9), it covers 4 weeks with respect to side effects. In three cases with LDH which went through six treatments with each of the above mentioned methods, both NPS was increased lower and SW with Cascadeflo EC-909W after apoE therapies.

- **Lysosomal hyperproteinaemia**
  - Lysosomes is a circulating lipoprotein that resembles LDL. Increasing levels of LDL in increase in risk of myocardial infarction (MI). Beneficial effect of LDL apoE in the incidence of major adverse coronary events (MACE) was observed in the retrospective study (6). Incidence of MACE in patients who have elevated LDL levels was evaluated for two years before and after commencement of LDL apoE in the prospective observational multicenter study. 101 cases with LDL apoE were enrolled. Incidence of MACE was significantly decreased from 32.9% in the last year before commencement of LDL apoE to 19.4% in the first year of DFPP apoE (P=0.02).

- **Organ Transplant**
  - HLA-A29-compatible kidney transplant
  - DFPP is an essential modality of anti-HLA antibody and anti-biopopulation removal in HLA-matched and A29-compatible kidney transplant. Anti-biopopulation mediated rejection (ABMR) is an important cause of acute and chronic rejection. In particular, the graft survival rate was comparable in patients with HLA-A29 and HLA-A29 compatible kidney transplant, which indicates that the condition of the patient who did not receive desensitization. The graft survival rate was improved to comparable to HLA-compatible cases (6).

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**Examples of Applications**
(based on Japanese health insurance coverage and references 5 and 14 to 17)

- **Metabolic Disorders**
  - Familial hypercholesterolemia (FH) **Lysosomal hyperproteinaemia**

- **Rheumatologic Disorders**
  - Systemic lupus erythematosus (SLE)

- **Neuropsychiatric Disorders**
  - Schizophrenia (MSD)

- **Neoplastic Disorders**
  - Primary malignant thrombosis (DTF)

- **Hematologic Disorders**
  - platelet disorder (HC)

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**Circuit Diagram**

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**Stable Sieving Coefficient**

Unique mechanism of resistant fiber avoids clogging, and enables stable performance.

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**Organ Transplant**
HLA-A29-compatible kidney transplant
- HLA-A29 incompatible kidney transplant
- Antibody-mediated rejection (AR)
**Separation Mechanism**

Phenol, obtained by PhenolSep OP and PhenolSep GP, is then fractionated into large and small molecules for weight components by Cascadefio EC using cation exchange components. Phases such as PhenolSep OP and PhenolSep GP are dissolved. Small molecules weight components being valuable antioxidants are finally separated to the light fractions.

**Selection of Models**

Use of EC-50W

- Area of Hematocrit (Hematocrit 50)
  - 50%: Higher performance than EC-0W
  - 25%: Lower performance than EC-0W

Use of EC-300W

- Area of Hematocrit (Hematocrit 50)
  - 30%: Higher performance than EC-0W
  - 20%: Lower performance than EC-0W

**Replacement Fluid**

- **Model**: EC-0W
  - Practical setting of replacement fluid condition
    - Not necessary

- **Model**: EC-50W
  - Discard 0% of processed plasma, replace with equivalent volume of saline solution

- **Model**: EC-300W
  - Discard 15% of processed plasma, replace with equivalent volume of saline solution

- **Model**: EC-300W
  - Discard 20% of processed plasma, replace with equivalent volume of saline solution

**Specifications**

- **Phenol Sep EC**
  - **Model**: EC-0W
    - **Column diameter**: 15mm
    - **Column length**: 300mm
    - **Flow rate**: 2L/min
  - **Model**: EC-300W
    - **Column diameter**: 15mm
    - **Column length**: 300mm
    - **Flow rate**: 3L/min
  - **Model**: EC-300W
    - **Column diameter**: 15mm
    - **Column length**: 300mm
    - **Flow rate**: 4L/min

**References**