AsahiKASEI

Cascadeflo™ XC

Asahi Plasma Component Separator for Double Filtration Plasmapheresis (DFPP)

- Minimal albumin loss & effective removal of target substances by selection of appropriate filter among the four different pore size models
- Bisphenol A (BPA) free

ASAHI KASEI MEDICAL CO., LTD.
A Pioneer in Blood Purification

Indication

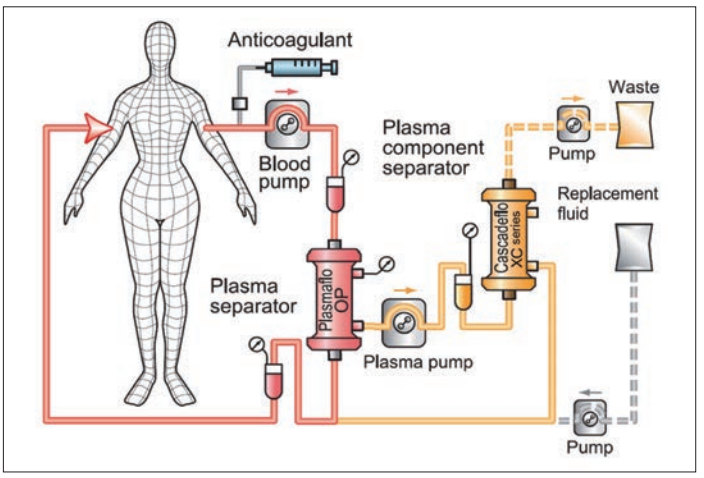
This device is applicable to diseases which have the causative factors or etiology in high molecular weight substances of plasma, such as

- metabolic diseases with XC-50 or XC-40
- autoimmune diseases with XC-30 or XC-20

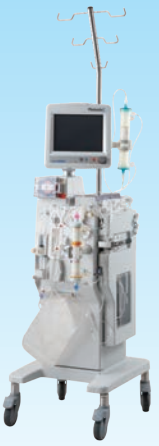
Features of Cascadeflo XC

- Wide applications by selection of optimal model
- Minimal loss of patient's own desirable non-pathogenic substances, e.g., albumin
- No or minimal risk of infection from replacement fluid
- Reduces possible protein allergy to replacement fluid

Circuit Diagram



Blood Purification Equipment

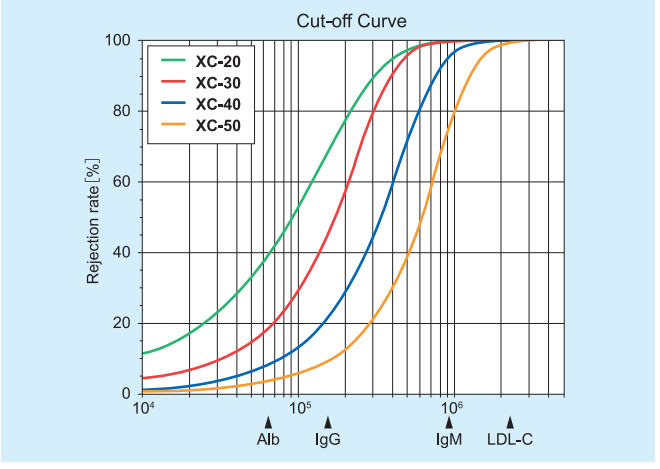


Plasauto Σ™

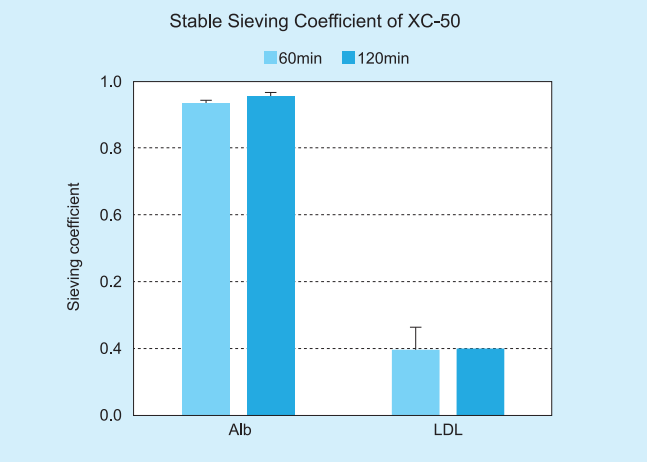
- Quick set up of the tubings
- Automatic flow rate control
- Automatic plasma recovery
- Extra option of Citrate Anticoagulation

Performance of XC

Unique microstructure of hollow fiber avoids clogging, and enables stable performance



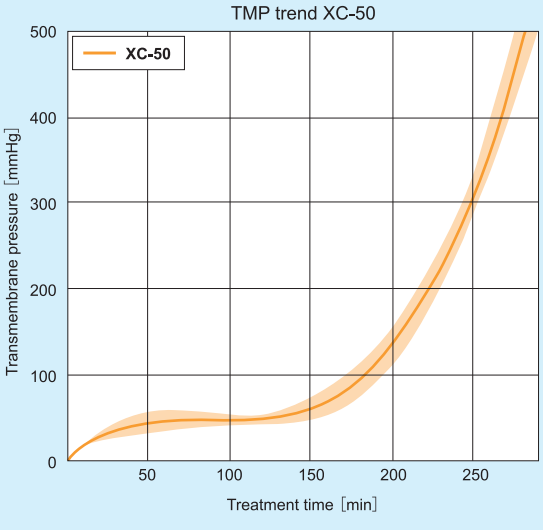
in vitro data, Bovine plasma : 3 L, TP : 6.0 g/dL
Plasma flow rate : 30 mL/min
Discard flow rate : 6 mL/min (XC-20), 3 mL/min (XC-30/40), 1 mL/min (XC-50)

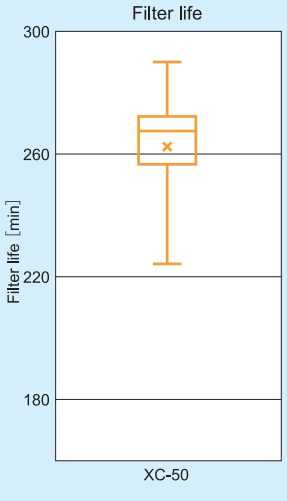


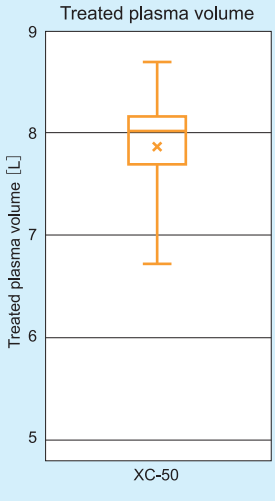
in vitro data, Bovine plasma : 3 L, TP : 6.0 g/dL
Plasma flow rate : 30 mL/min
Discard flow rate : 1 mL/min

Performance of XC

Unique microstructure of hollow fiber avoids clogging, and enables stable performance







in vitro data, Bovine plasma : 4 L, TP : 6.0 g/dL
Plasma flow rate : 30 mL/min
Discard flow rate : 0 mL/min

Clinical Experiences of DFPP

DFPP can be applied to a variety of refractory disorders including metabolic disorders, organ transplants, rheumatic disorders, dermatologic disorders, and neurological disorders by selecting the optimal plasma component separator model [1]. The clinical experiences in typical disorders are described below.

<Metabolic Disorders>

Familial hypercholesterolemia (FH)

LDL apheresis is applied for FH patients who have either ineffective or ill tolerated maximum medication therapy and ineffective dietary control. LDL cholesterol (LDL-C) can be removed from plasma by DFPP, adsorption, or precipitation or from whole blood. A study compared three different LDL apheresis columns (DL-75, LA-15, Cascadeflo) with respect to side effects (SE) in three cases with FH who went through six treatments with each of the aforementioned methods, finding a significant fewer SE with Cascadeflo after apheresis [2].

Lp(a) hyperlipoproteinemia

Lp(a) is a circulating lipoprotein that resembles LDL-C. Increasing levels of Lp(a) increase in risk of myocardial infarction [3]. Beneficial effect of LDL apheresis in the incidence of major adverse coronary events (MACE) was observed in the retrospective study [4]. Incidence of MACE in patients who have elevated Lp(a) level was evaluated for two years before and after commencement of LDL apheresis in the prospective observational multicenter study. 101 cases with DFPP were enrolled. Incidence of MACE was significantly decreased from 0.52 in the last year before commencement of DFPP to 0.12 in the first year of DFPP ($p<0.0001$) [5].

Clinical Experiences of DFPP

<Organ Transplants>

HLA-/ABO-incompatible kidney transplant

DFPP is an established modality of anti-HLA antibody and anti-blood group removal in HLA-incompatible and ABO-incompatible kidney transplant. Antibody mediated rejection (AMR) is an important cause of acute and chronic allograft dysfunction and graft loss. Desensitization protocol including DFPP and rituximab before transplant was performed in 52 cases with HLA-incompatible living donor kidney transplant. The incidence of acute and chronic AMR was significantly reduced (p=0.005 and p=0.004, respectively) compared to 24 cases who did not receive desensitization. The graft survival rate was improved to comparable to HLA-compatible cases [6].

<Rheumatic Disorders>

Systemic lupus erythematosus (SLE)

DFPP is effective for eliminating pathogenic molecules such as anti-DNA antibody and immune complexes in SLE patients. Clinical benefit of apheresis (DFPP or immunoadsoption) was evaluated in lupus nephritis (LN) patients in three groups, i.e., apheresis group (9 cases), intravenous cyclophosphamide pulse therapy (IVCY) group (16 cases), and combination of apheresis and IVCY group (13 cases). Complete remission rate was comparable in apheresis and IVCY groups, while combination group had higher complete remission rate. Combination therapy may be superior in achieving the complete remission of LN, and in minimizing the risk of adverse effects of IVCY [7]. 24 LN patients were divided into two groups (DFPP group and control group). DFPP group received 3 sessions of DFPP in combination with methylprednisolone. In the DFPP group, remission was accelerated, total glucocorticoid doses were reduced, relapse was prevented, and higher C3 levels than in the control group [8].

<Dermatologic Disorders>

Pemphigus, Pemphigoid

Pemphigus is an autoimmune skin blistering disease in which desmoglein, an epidermal cell adhesion molecule is targeted by autoantibodies. Pemphigoid is an autoimmune skin blistering disease caused by antidermal basal lamina antibody. Medication in Pemphigus and Pemphigoid includes the administration of corticosteroids, immunosuppressants and IVIg. DFPP is applied for patients who is resistant to medication or patients suffering from complications of medication. 4 cases in pemphigus foliaceus and 1 case in pemphigus vulgaris [9] and 3 cases in pemphigoid [10] received series of DFPP, resulted in an improvement in clinical symptoms and remission.

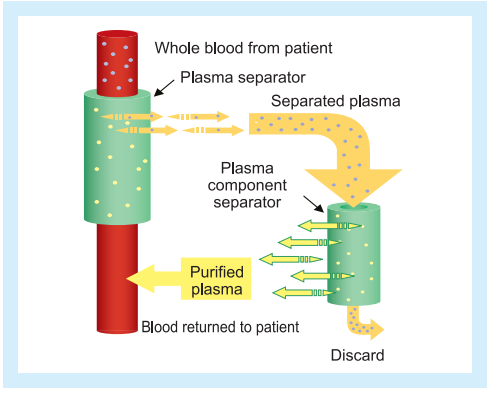
<Microcirculatory Disorders>

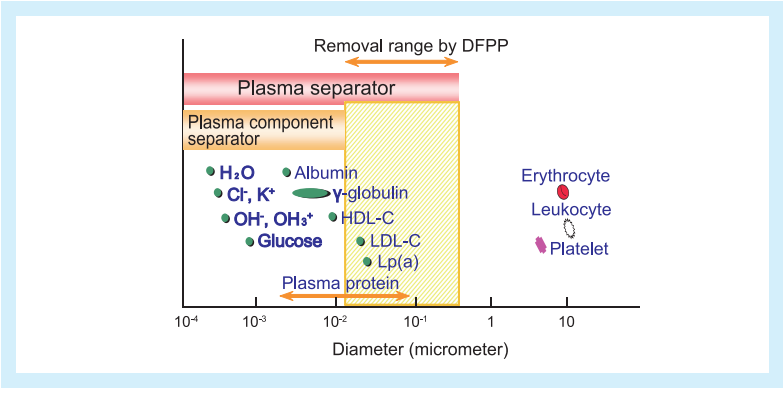
Peripheral arterial disease (PAD)

By eliminating LDL particles and high molecular weight proteins, DFPP decreases plasma viscosity and thereby improves hemorheology in microcirculation [11]. 28 hemodialysis patients with chronic limb-threatening ischemia received a median of 15 DFPP sessions (6 to 86 sessions). 20 (71.4%) patients experienced complete wound healing during follow-up. Fibrinogen, C-reactive protein, α2-macroglobulin, TC, LDL-C, HDL-C, TG, IgM, and estimated plasma viscosity were significantly reduced (P<0.0001) [12]. 8 cases with non-healing foot ulcers caused by severe ischemic diabetic foot syndrome underwent 7 DFPP sessions. Wound healing was accelerated in 4 cases and was unchanged in 2 cases, but with an increase in tcpO2 that allowed successful minor amputation [13].

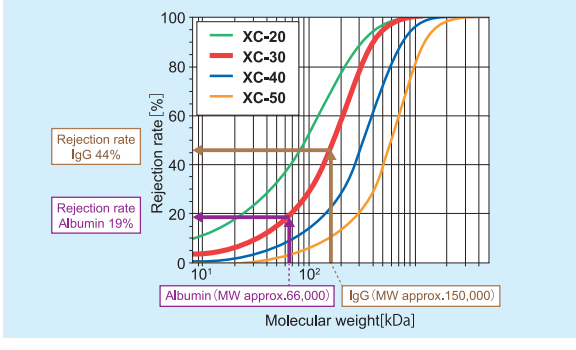
Separation Mechanism

Plasma, obtained by Plasmaflo OP is then fractionated into large and small molecular weight components by Cascadeflo XC. Large molecular weight components including pathogenic substances such as IgG and LDL-C are discarded. Small molecular weight components including valuable substances such as albumin are returned to the patient.





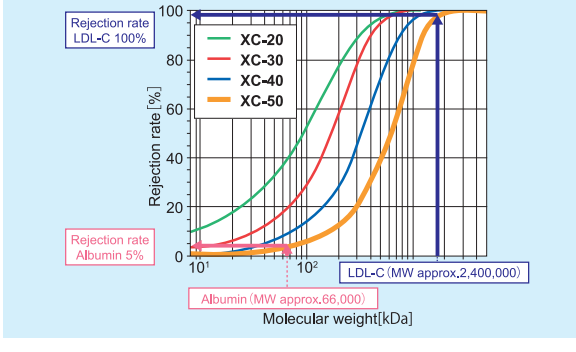
Selection of Models



Use of XC-30

XC-30 is used mainly for IgG removal. 44% of IgG can be removed using XC-30 based on the rejection rate of IgG (molecular weight (MW) approx. 150,000).
Since 19% albumin (MW approx. 66,000) is removed, replacememt fluid such as albumin solution is necessary to compensate for the removed albumin.
Note: XC-20 has a higher removal performance than XC-30, and a higher possibility of filter clogging. Albumin removal is higher, and a larger amount of replacement fluid is necessary.

in vitro data, Bovine plasma : 3 L, TP : 6.0 g/dL
Plasma flow rate : 30 mL/min
Discard flow rate : 3 mL/min

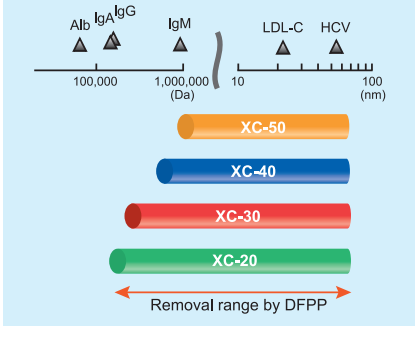


Use of XC-50

XC-50 is mainly used for LDL-C removal.
Approx. 100% of LDL-C can be removal using XC-50 based on the rejection rate of LDL-C (MW approx. 2,400,000). Albumin removal is only 5%, and albumin replacement is NOT necessary.

in vitro data, Bovine plasma : 3 L, TP : 6.0 g/dL
Plasma flow rate : 30 mL/min
Discard flow rate : 1 mL/min

Replacement Fluid



Model	Practical example of replacement fluid condition
XC-50	Not necessary
XC-40	Discard 0 - 10% of processed plasma, replace with equivalent volume of saline solution. Take care of albumin level when treatments are performed every day or every other day.
XC-30	Discard 10% of processed plasma, replace with equivalent volume of 5% albumin solution.
XC-20	Discard 20% of processed plasma, replace with equivalent volume of 12% albumin solution.

Specifications

	XC-20	XC-30	XC-40	XC-50
▲ Hollow fiber Materia	Ethylene vinyl alcohol copolymer			
Inside diameter	175μm			
Wall thickness	40μm			
Surface area	2.0㎡			
Priming volume plasma side / filtration side	110/200mL			
▲ Container Material	Styrene-butadiene block copolymer			
Dimensions	334mm [L] × 47mm [D]			
▲ Sterilization	Gamma-Ray			

XC-20 is the smallest pore size model, and XC-50 is the largest pore size model

References

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3) Kamstrup et al. Extreme lipoprotein(a) levels and risk of myocardial infarction in the general population: the Copenhagen City Heart Study. Circulation. 117:176-84,2008.

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