MICRODYN
Capillary Cartridges

User Manual

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1 Introduction

MICRODYN capillary cartridges contain a bundle of capillary membranes that maximizes the size of the effective filtration area and provides a long filter service life at low differential pressure during operation. It is constructed as an exchangeable cartridge and fits into special stainless steel housings.

The polypropylene membrane has a defined pore structure and a high porosity of about 75%. The membrane has excellent solvent and acid/base resistance and is a barrier for bacteria and submicron particles with a nominal pore size of 0.1 µm or 0.2 µm.

MICRODYN capillary cartridges have been developed for crossflow microfiltration (CMF), a modern filtration procedure for separating suspended or emulsified particles in the range of 0.1 - 100 mm. The separated particles form a deposit layer on the membrane surface, which is reduced to a limited thickness by means of:

a) shear forces at the membrane surface due to tangential flow and
b) periodic backwashing (PBW) of the membrane in opposite direction to the filtrate flow.

Both procedures can easily be realized by the self-supporting capillary membranes.

The favorable flow velocity inside the capillaries ranges from 0,5 to 3 m/s. Backflushing intervals of 1 to 30 minutes are recommended depending on the product. For applications requiring sterilization, the MD070 cartridges can be steam sterilized in its housing for 30 minutes at 121°C (250°F) for up to 10 times. Polypropylene membranes are hydrophobic, which requires an activation of the cartridge for filtration of water and aqueous solutions (see Section 4).

2 Product Description

2.1 CARTRIDGE DESIGN

A bundle of capillaries is potted at both ends to an outer support with end caps. A double O-ring seal protects against cartridge by-pass in the housing. To allow for sterilization, the cartridges contain a metallic support ring at the end cap.

Normal filtration direction is from inside to outside.

2.2 MATERIALS USED

The materials of construction are:

Membrane:	Polypropylene
Support cage:	Polypropylene
End caps:	Polypropylene and stainless steel support ring
Potting:	Polyurethane
O-rings:	Ethylene Propylene Copolymer (EPDM)

2.3 DIMENSIONS & OPERATIONAL DATA

The main dimensions and operational parameters of MICRODYN cartridges are shown in Table 1. Please note that only MD070 series can be heat sterilized.

TABLE 1. Cartridge Dimensions

	MD070 CP 2L	MD070 FP 1L	MD070 FP 2L	HC 02 54 B 21
Cartridge length [mm]	560			
Cartridge diameter [mm]	72	72	72	76
Capillary inner diameter [mm]	1.8	0.6	0.6	0.6
Pore size [µm]	0.2	0.1	0.2	0.2
Membrane area based on fiber inner diameter [mm]	0.9	2.2	2.2	2.4
Flowrate at 1 m/s [l/h]	3200	2650	2650	3060
Operating temperature [°C]	5-40	5-40	5-40	5-35
Max transmembrane pressure inside-out [bar] @25°C	1.6	1.6	1.6	2.0
Max transmembrane pressure inside-out [bar] @40°C	1.4	1.4	1.4	1.5
Max back pulse pressure above concentrate pressure [bar] @25°C	1.0	1.0	1.0	1.5
Max back pulse pressure above concentrate pressure [bar] @40°C	0.5	0.5	0.5	1.0
Heat sanitization	10 x for 30min @121°C	10 x for 30min @121°C	10 x for 30min @121°C	NO

3 Biocompatibility

All materials of MICRODYN capillary cartridges have been evaluated and documented for biosafety in accordance with the USP Class VI Plastics Tests to ensure safety of materials.

The individual plastic components were analyzed by a State Registered Expert according to the guidelines for testing of plastics, when used as consumer products with the reference to the LMBG, including 50th memorandum, Bundesgesundheitsblatt 30, 368 (1987), dated Oct. 1987, as well as in accordance with DAB9 VI.1.2.2.3., 155,1.2.2., 156/157 and methods V.6.

The filter units correspond to the German Foodstuff and Consumer Products Law - dated 15.08.'74, §§ 30 and 31, and are admitted according to the recommendations VII, XXXIV and XXI of BGA.

In such as all the components of the filtration cartridges are in full compliance with the relevant FDA requirements, and since the stainless steel used in the cartridge housing is recognized as safe for use in contact with pharmaceuticals, MICRODYN capillary cartridges are in full compliance with the Federal Food, Drug and Cosmetic Act and the applicable Food Additive Regulations: 21 CFR Ch.I §§ 177.1520, 177.1620 and 177.2600.

Detailed documents covering this matter are available on request.

4 Operating the Cartridges

4.1 ACTIVATION

Due to the hydrophobic character of the polypropylene membrane, activation (pre-wetting) of the membrane is necessary. Wetting is possible by means of water-soluble liquids with a surface tension of less than 0.035 N/m. Appropriate liquids include ethanol, isopropanol, mixtures of water with at least 50 vol. % of isopropanol, or mixtures of water with at least 25 vol. % of tertiary butanol. The latter mixture is generally not flammable, but please note that the vapor of the solution has a flash point in open air of approx. 25°C.

After the activation procedure, the module is rinsed either with water or with the solution to be filtered.

4.2 STERILIZATION

MICRODYN capillary type MD070 cartridges withstand 10 cycles of in-line steam sterilization with saturated steam at 121°C for 30 minutes.

Please note that heat sterilization is only allowed for MD070 series. HC 02 54 B 21 cartridges cannot be heat sterilized.

The transmembrane pressure must not exceed 100 mbar (close permeate valve to prevent TMP build-up). The differential pressure along the module must not exceed 200 mbar. The modules may also be sterilized by autoclaving (either wet or dry).

Chemical sanitization can be done under the following conditions:

1. Formaldehyde; 0.5vol% for 20 minutes.
2. Hydrogen Peroxide; 2vol% for 20 minutes.

Appendix 6.1 shows an example of a sterilization with measured diffusion flows before and after sterilization.

4.3 OPERATING PRESSURE AND TEMPERATURE

In considering crossflow microfiltration, a liquid is pumped through the MICRODYN cartridge. The normal filtration direction is from the capillary inside to the outside. The hydraulic pressure drops from the inlet value p_{inlet} over the length of the capillary to the outlet value p_{outlet} due to the liquid flow rate inside the capillary membranes. The pressure drop depends on the crossflow velocity. Figure 1 shows the pressure drop for the MD070 FP 2L with water at 20°C.

During crossflow filtration, the filtrate pressure p_F must be lower than the outlet pressure P_{outlet} at any time. When operating in backflushing mode, the filtrate pressure p_F must increase to a value higher than the inlet pressure p_{inlet} for a short time.

The maximal operating pressures (p_{inlet} - $p_{filtrate}$) and back pulse pressures ($p_{filtare}$ - p_{outlet}) at 25°C and 40°C are listed on the specific data sheets.

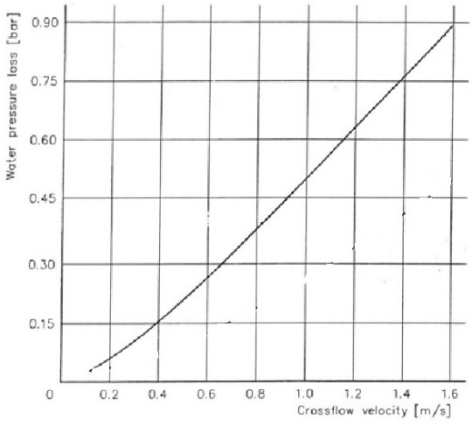

Figure 1. Pressure loss vs. cross flow for MD070 FP 2L.

5 Chemical Compatibility

The materials used are resistant to aqueous salt solutions, diluted inorganic acids as well as diluted and concentrated caustic solutions. They are not resistant to oxidants. Aromatic and aliphatic hydrocarbons with low boiling point (e.g. petrol ether, benzene, and carbon tetra-chloride) diffuse into the polymers and produce swelling and decreasing consistency. An exception are non-volatile substances (e.g. grease, oil, and wax); they cause negligible swelling and slow decay only.

The following schedule lists the resistance of MICRODYN capillary cartridges with PP membranes. The resistance depends on many factors (e.g. temperature, concentration, and intensity of the mechanical stress). The data in the list acts as a first orientation only. Table 2 considers the cartridge materials polypropylene and polyurethane.

Symbols: + resistant operating conditions as per data sheet
/ limited resistance, swelling limited operating conditions
- not resistant

Table 2. Chemical Resistance

Chemical	Resistance	Chemical	Resistance	Chemical	Resistance
Acetic acid, 10%	+	glycerol	+	starch solution	+
Acetone	/	hydrofluoric acid, 10%	/	tartaric acid, aqueous, 10%	+
Amylic alcohol	-	glycol	+	toluene	-
Aniline	-	hexane	/	trichlorethylene	-
Benzene	-	isopropanol	+	trichloro acetic acid	/
Beer	+	juices, aqueous	+	turpentine	-
Bromic water, cold saturated	-	lactic acid, aqueous, 10%	+	vinegar	+
Butanol	/	linseed oil	+	water	+
Butyl acetate	/	mechanical oil	/	whisky	+
Butyl glycol	+	methanol	+	xylol	-
Calcium chloride sol. (aqueous)	+	methylenchloride	-		
Carbon tetrachloride	-	molasses	+		
Hydrochloric acid, 10%, aqueous	+	mineral oils	+		
Chlorobenzene	+	mineral water, commercial qual.	+		
Chloroform	-	milk	+		
Chlorosulfonic acid	-	nitric acid, (2n), aqueous	/		
Hydrochloric acid, 30%, aqueous	+	nitrobenzene	-		
Salt water	-	oleum, 100%	-		
Citric acid, aqueous, 10%	+	olive oil	+		
Cyclohexane	/	peracetic acid, 0.2 %	-		
Cyclohexanol	/	petrol ether	+		
Cyclohexanone	/	petrol ether, Kp 100 - 140 C	/		
Diethanol amine	+	plant oils	+		
Dichloroethylene	/	potassium hydroxide, aqueous	+		
Dichlorobenzene, cold sat.	/	potassium permanganate (2n)	/		
Dimethylamine	/	pyridine	-		
Ethanol, 99%	+	saline, saturated	+		
Ethyl acetate	-	sea water	+		
Ethyl ether	-	silicon oil	+		
Ethylene glycol	+	soap solution	+		
Ethyl acetate	-	sodium carbonate solution			
Ethyl ether	-	cold saturated, aqueous	+		
Ethylene glycol	+	sodium sulfite, 40%	+		
Ferrous chloride (III), sat.	+	sodium hydroxide solution (2n)	+		
Formic acid (dil.)	+	sodium hydroxide solution, 52%	+		
Formaldehyde, 30%, aqueous	+	soybean oil	+		
Freon, aqueous, cold sat.	+	sulfuric acid (2n), aqueous	+		
Fruit juices	+	sodium carbonate solution	+		
Galvanic baths	+	cold saturated, aqueous			
Gelatin	+	sodium sulfite, 40%	+		
Glucose, aqueous	+	sulfuric acid (dil.)	+		

6 Appendix

6.1 EXAMPLE OF DIFFUSION FLOW BEFORE AND AFTER STERILIZATION (APPLIES FOR MD070 SERIES)

The test procedure comprises:

1. Saturated steam of 121°C (2 bar) for 30 minutes per cycle, measured by a gauge installed downstream.
2. 100 - 200 mbar pressure difference between upstream and downstream gauges, trans-membrane pressure <100 mbar.
3. More than 10 cycles per test.
4. Cooling to room temperature between cycles.
5. Integrity tests by diffusion method before and after the cycles.

Some results for the cartridge type with membranes I.D./O.D.= 0,6/1,0 mm are listed in Table 3, which confirms that no loss of integrity has occurred under the conditions described above.

Table 3. Integrity Before and After Sterilizability Test

Cartridge serial number	Diffusion flow before test [ml/min]	Diffusion flow after test [ml/min]
8709059	16	14
8709060	8	5
8709061	5	17
8709063	0	3
8709064	8	15
8709065	12	20
8709066	4	12

6.2 BACTERIA RETENTION AND INTEGRITY TESTING

Bacteria Retention

MICRODYN cartridges are of sterilizing grade as tested and confirmed, following the established guidelines of the HIMA document no.3, vol.4.

Following the guidelines, the 0.2 µm cartridges are challenged with a bacteria suspension of Pseudomonas diminuta (ATCC no. 19,146) cultivated in a saline lactose broth.

For 0.1 µm cartridges, Acholeplasma laidlawaii are used (ATCC no. 23,206). The cartridges are wetted and sterilized in isopropanol, 70% (vol.%) for 60 minutes. Subsequently, the cartridges are washed with 5 liters of ultrapure water prior to filtration. The bacteria suspension is filtered through the cartridge so that the effective membrane area is contaminated with at least 107 organisms per cm^2.

The filtrate passes through an analytical disc filter, which is then placed on a soybean casein digest agar and incubated for seven days. Finally, the disc is inspected for colonies that can be identified as Pseudomonas diminuta. Sterilizing grade is confirmed if no Pseudomonas diminuta bacteria are detected on the analytical disc.

Typical test results with cartridges of type MD070 are reported in Table 4. In the last column of this table, the log reduction values (LRV) are listed. This is the logarithm (to the base 10) of the ratio of total organisms in the challenge to the organisms in the filtrate:

$$LRV = \log \frac{\text{number of organisms in challenge}}{\text{number of organisms in filtrate}}$$

When the filtrate is sterile, 1 is substituted in the denominator thus reading:

LRV > log (number of organisms in challenge).

Bubble Point Test

Since a microbiological retention test is complicated and, moreover, even a destructive method (the cartridge must be disposed), it is necessary to employ a non-destructive integrity test.

One of the methods usually applied is the "bubble point test," especially for membrane samples (production control) or small filter units. This test is based on the principle of capillary forces.

It is performed by wetting the membrane completely with a suitable liquid (see activation section) and then applying a slowly increasing pressure of air or nitrogen in the filtration direction until a continuous stream of bubbles in the liquid at the other side of the membrane indicates that the capillary attraction has been overcome and the liquid has been forced out of the largest pore. The maximum pore size can easily be derived from this bubble point pressure with the following equation:

$$dp = K/pB$$

dp = max. pore size (µm)
pB = bubble point pressure (bar)
K = Constant (depending on test liquid)
0.633 (bar mm) for ethanol and isopropyl alcohol (IPA)

Experience shows that there exists a good correlation between the microbiological retention test and the bubble point pressure and maximum pore size, respectively. The maximum pore sizes of 0.2 µm membranes are 2 -3 times larger than the rated pore size. Table 4 lists these approx. values with the challenge results.

Diffusion Test

For larger filter units or filtration equipment where bubbles cannot be observed, another test method is usually applied (i.e. the "diffusion test").

In principle, an activated filter is pressurized with N_2 at about 80% of the bubble point pressure while the gas flow through the membrane is measured. This gas flow is caused by diffusion through the liquid. The diffusional flow of a qualified cartridge does not exceed a value previously determined.

Every MICRODYN cartridge is tested by this method before delivery.

Table 4. Bacteria Retention Test Data and Maximum Pore Sizes for Cartridges with Capillary Membranes I.D.O.D. = 0,6/1,0 Mm and Different Max. Pore Sizes

Cartridge serial number	Max pore size [µm]	Number of organisms in challenge	Number of organisms in filtrate	LRV
86110001	0.55	$7.5x10^{13}$	0	> 13.9
86110002	0.52	$7.5x10^{13}$	0	> 13.9
86110003	0.52	$4.3x10^{10}$	0	> 10.6
86110005	0.54	$3.1x10^{11}$	0	> 11.5
86110007	0.54	$2.6x10^{11}$	0	> 11.4
86110010	0.54	$2.5x10^{9}$	0	> 9.4
86110057	0.57	$5.0x10^{11}$	0	> 11.7
86110059	0.51	$3.4x10^{11}$	0	> 11.5
86110075	0.56	$6.9x10^{11}$	0	> 11.8
86110835	0.63	$6.8x10^{11}$	0	> 11.8
86110838	0.63	$6.8x10^{11}$	0	> 11.8
86110845	0.64	$3.3x10^{11}$	0	> 11.5
86110834	0.70	$5.8x10^{11}$	<300	< 9.3
86110839	0.69	$5.0x10^{11}$	<300	< 9.2

NOTE: These results indicate that the maximum pore size, determined by the bubble point test, should not exceed a value of about 0.65 µm.