The film adsorber : a new developed artificial organ to remove exogenous and endogenous poisons from blood

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PROEFSCHRIFT

DOOR

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GEBOREN TE UTRECHT

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aan mijn ouders

SUMMARY

In this thesis the development and analysis of a new type
of adsorber (the film adsorber) is described for the use as
an artificial organ to remove exogenous and endogenous poi-
sons from blood.
The film adsorber can be used among other applications:
1 as an addition to the hemodialyser
2 as adsorber in cases of acute hepatic failure
3 as adsorber in cases of autointoxications.
For each of these applications the film adsorber can be op-
timized by using different materials or dimensions.
A technological analysis of the film adsorber was performed
with the following results:
1 analysis of the flow pattern revealed, that the film ad-
  sorber containes neither short circuits nor dead corners
  of importance.
2 by means of an integration of the different masstransfer
  mechanisms a reasonable approximation can be made of both
  the number of masstransfer units and the mean residence
  time.
3 when the film adsorber is flown through by bovine blood,
  the pressure drop over the adsorber can be described by
  the formula of the pressure drop over a slit for a Cas-
  sonian fluid with the assumption of a marginal plasma
  layer.
For the applications mentioned above the film adsorber comes
in direct contact with the blood of a patient. Therefore
preclinical analysis was carried out. This showed, that
1 in the film adsorber all carbon particles are covered by
  a collodion layer
2 neither carbon particles nor glass beads are released by
  the film adsorber
3 the damage to erythrocytes is negligible
4 all metabolites are adsorbed except urea

5 the clearance of barbiturates is much higher than the clearance obtained either by forced diuresis of by means of a dialyser
6 the film adsorber is an useful addition to the hemodialyser. Not only the clearance of metabolites with a molecular weight between 100 and 200 is increased by simultaneous use, but also the clearance of the middle molecules is increased

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CURRICULUM VITAE

The author was born on March 27, 1947 in Utrecht, The Netherlands. Following his secondary education at the gymnasium of the Openbaar Lyceum "Scoonoord" in Zeist, he began his studies in the Chemical Engineering Department at the Technische Hogeschool Eindhoven in 1965. Graduate work leading to the title of "scheikundig ingenieur" in March 1971 was performed under the guidance of prof.dr. K. Rietema. From March 1971 until March 1974 he was "wetenschappelijk assistent" in the dapartment of "Fysische Technologie under the direction of prof.dr. K. Rietema.

CONTENTS

CHAPTER I

INTRODUCTION

Dialysis of blood in case of renal deficiency was first
applied by Kolff and is now more than 30 years old.
Although many improvements in apparatus and membranes and
also in control and technique have been achieved since
its first application the principle of artificial blood
purification is still the same at the present time.
Of course an artificial kidney can never replace all the
functions of a real kidney, but by means of dialysis the
main metabolic products, excessive water and unwanted
ions can be removed. Drawbacks of dialysis are still the
large sizes of the equipment, the large amount of dialy-
sate needed to extract the metabolites and the long time
necessary for each treatment especially because of the
poor extraction capacity for the so called middle mole-
cules (M>200).
For 10 years they have tried to find an alternative for
dialysis on basis of the principle of adsorption in which
activated carbon is contacted directly or indirectly with
the blood. Molecules with a molecular weight larger than
70 are good adsorbed to the carbon. This principle could
be further extended by means of chemical or enzymatic
conversion and adsorption of ions to ionexchangers.
Chang was the first to apply clinically an artificial
kidney on basis of adsorption. In order to prevent blood
damage by the direct contact between blood cells and car-
bon particles he encapsulated the carbon particles in a
collodion film by means of a precipitation technique. The
encapsulated carbon particles (average size about 2 mm)
are packed in a cylinder of about 600 cm^3, which is taken
up in a extracorporal blood shunt.
All metabolic products except urea, water and ions are
removed in this way. Adsorption of the very large protein

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molecules is prevented by means of the semipermeable collodion membranes around the carbon particles.

Although no doubt Chang had some succes, his technique is far from perfect:

1. Encapsulation of carbon particles by means of the precipitation is very difficult and never complete. Especially for smaller particles the encapsulation is only partly. Particles smaller than about 2 mm in diameter can not be used so that a large amount of particles is necessary to obtain a sufficient large exchanging surface (in Chang's apparatus circa 1 m^2).

2. The more or less random packing of the carbon particles causes a stochastic spread of the blood flow over the particles: some particles are in good contact with the blood flow, while other particles or parts of the surface are captured in dead corners; also channeling especially along the cylinder wall is possible.

3. The strongly tortured blood flow streamlines cause a relative high pressuredrop over the artificial kidney.

4. Because of the large amount of carbon particles necessary to obtain a sufficiently high exchanging surface area also the blood holdup (priming volume) is high (300 cm^3).

In this thesis the use of an adsorber, with a new design, for the removal of endogenous and exogenous poisons from blood will be discussed. Especially, however, the use for the treatment of uremic patients will be discussed.

To understand the development of an adsorber for this purpose, the functions of the natural kidney will be discussed in paragraph I-1 and the principles of the hemodialyser in paragraph I-2.

Moreover the possiblities of the adsorber will be described in paragraph I-3.

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I-1 <u>The human kidney</u>

The human kidney has the following functions:

<u>a</u> The removal of the non volatile metabolic products and
   dietetic substances from the blood. These products are
   among others urea, uric acid, creatinine and detoxifica-
   tion products. For a more complete list of these pro-
   ducts see table I-1.

<u>b</u> The metabolic regulation of the acid-base equilibrium of
   the body fluids (e.g. H^+ elimination)

<u>c</u> An important contribution to the electrolyt- and water-
   balance of the body.

<u>d</u> The production of hormones:
   - erythropoetine, which stimulates the production of
     hemoglobine
   - renine, which has a function in the regulation of the
     blood pressure.

The functions <u>a</u>, <u>b</u> and <u>c</u> take place in the 10^6 nephrons
of each kidney. Each nephron is capable of producing urine.
Such a nephron is schematically sketched in figure I-1.
The blood enters the glomerulus (g) of the nephron through
the arteriole (a) and flows through peritubular capilla-
ries (p) surrounding the tubule of the nephron back into
the vein (v). The glomerulus consists of a network of pa-
rallel capillaries (c) held in the Bowmans capsule (B).
The mass transfer across the capillaries is caused by ul-
trafiltration due to the static pressure across the capil-
laries decreased with the intracapsular pressure and the
colloidosmotic pressure in the arteriole.
The ultrafiltrate (normally about 200 l/day) containes
only molecules with a molecular weight smaller than about
15000. It is for about 70% reabsorbed in the proximal tu-
bule (t). The residue passes through the loop of Henle (H)
and comes via cells lining the distal tubule (d) in contact
with the blood in the peritubular capillaries. During this
contact a selective reabsorption and secretion takes place.

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The cells are filters, each with a task to reabsorb a
particular solute necessary for the body.
Most of the water goes back to the blood. Daily about 99%
of the 200 l is reabsorbed. The residue of the ultrafil-
trate, the urine, flows into the bladder.
Renal insufficiency is the result of loss of kidney func-
tion mostly by damage of any part of the nephrons. Gene-
rally more than about 90% of the function of both kidneys
must fall out before symptoms of illness arise such as:
weariness, apathy, disturbances of equilibrium, vomiting
and haemorrhage.
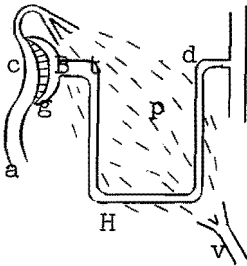
g glomerulus
a arteriole
p peritubular capillaries
v vein
c parallel capillaries
B Bowman's capsule
t proximal tubule
H loop of Henle
d distal tubule

figure I-1 the nephron

I-2 The hemodialyser

In case of renal insufficiency an artificial kidney toge-
ther with a dietetic regime has to fulfil the functions a,
b and c of the human kidney. The conventional artificial
kidney based on the principle of dialysis and ultrafil-
tration is called hemodialyser.

I-2-a the principle of the hemodialyser

The dialysis treatment involves, that a part of the blood
from a patient is extracorporally directed through the

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hemodialyser and back into the corporal blood circulation. In the hemodialyser the blood flows along a semipermeable membrane separating the blood from a special aqueous solution called the dialysate (see figure I-2).
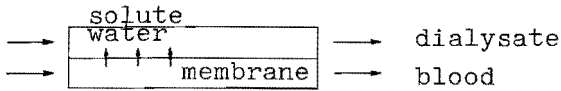
figure I-2 the hemodialyser

The normal composition of the dialysate is given in table I-1. The volume of dialysate needed for each treatment is minimal 200 litres. The temperature of the dialysate is so adjusted, that the blood flowing back into the patient has a temperature of 37°C.

Table I-1 the composition of the dialysate compared with the blood plasma, and the secretion per day

solute	dialysate	plasma (normal)	excretion per day
	concentrations in mmol/l		normal feed (g)
Ca^{++}	1,5	2,2 - 2,6	0,3 - 0,5
Mg^{++}	0,65	1,5	0,2 - 0,4
K^+	2	3,6 - 5	2 - 4
Na^+	130	138 - 144	4 - 7
Cl^-	100	100 - 105	10 - 15
acetate	35		
glucose	3	3,7 - 5,6	
uric acid	0	0,24	0,8
creatinine	0	0,08	1 - 2
urea	0	5	25 - 40

We can distinguish between compounds that:

a should_be removed

The metabolic products are removed by diffusion across the membrane into the dialysate. The concentration of these products in the dialysate is zero.

b should_be partly_removed

Substances, which are normal of importance, but which concentration may be elevated in uremia, have to be partly removed (e.g. K^+, phosphate and water). The pH- and the electrolyt balance is regulated by adjusting the dialysate (see table I-1).

c should_not_be removed

These compounds are among others blood cells and plasma proteins. From these the cells and the macro molecules (proteins) cannot pass the membrane. Others like hormones, fat soluble vitamins, trace elements, Fe and Cu are mainly adsorbed by the plasma proteins.

d should_be added

E.g. glucose and vitamins (orally).

The increased H^+ concentration (acidosis) is eliminated be the acetate in the dialysate, since acetic acid will disappear as such in the metabolism.

The surplus of water is removed by ultrafiltration caused by a pressure difference between the blood and dialysate compartment of the dialyser. The osmolarity of the dialysate is generally adjusted by variation of the concentration of glucose in the dialysate.

I-2-b the practical restrictions_of the hemodialyser

Since the use of a hemodialyser requires, that a part of the blood is led through an extracorporal shunt and since water and the metabolites are removed from the blood there are some limitations and requirements in the use of the hemodialyser.

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1 During the treatment the blood flows from a connection
placed in an artery of arm or leg through plastic tu-
bing and through the hemodialyser to another connection
placed in the vein.
To prevent clotting of the blood an anticoagulant (hepa-
rin) is infused continuously into the blood circuit be-
fore the dialyser. If necessary the heparin may be neu-
tralised by an infusion of protamine chloride after the
hemodialyser (regional heparinisation).
2 The extracorporal blood volume should be less than
500 ml.
3 High shear rates will cause damage of blood cells (he-
molysis). Therefore blood flow rates should be less than
300 ml/min in most dialysers, although this maximum
blood flow depends on the construction of the apparatus.
4 Theoretically it is possible to remove via the dialyser
any metabolite from the blood at high rates e.g. by in-
creasing the membrane surface area and/or the permeabi-
lity of the membrane.
A removal of the water and solutes, which is performed
too rapidly, however, may cause various disturbances in
the patient. Since the diffusion rates of metabolites
from the cells in the body towards the interstitial fluid
and further from the interstitial fluid towards the blood
are restricted, a dialysis implemented too rapidly may
cause an inacceptable osmolarity difference between the
cells and the interstitial fluid respectively the blood.
This difference may cause a swelling and subsequently
dammage of the cells (especially in the brain). This
phenomenon is known as desequilibrium syndrome and espe-
cially caused by a removal of urea and ions, which is
performed too rapidly.
If a metabolite is mainly removed from the blood the body
may extravasculary still contain much of the same solute,
since the blood volume is only 10-15% of the total body

fluid (40 l). Thus the fact, that the blood hardly con-
taines this solute anymore, does not include, that the
body is free of the solute.

5 After each dialysis treatment an amount of blood is lost
extracorporally a from blood sampling necessary for con-
trol and b because a rest volume of blood will always
remain in the dialyser after the treatment.

6 The production of hormones is not fulfilled by the arti-
ficial kidney and there is no way to fulfil this func-
tion at all. The problems, which might arise through
shortage of these hormones can only be solved by care-
ful medical control.

I-2-c the efficiency of the dialyser

To indicate the effect of an artificial kidney medical
specialists commonly use the dialysance defined as:

$$D=\frac{(C_{bi}-C_{bo})}{(C_{bi}-C_{di})}Q_b \qquad ml/min \qquad\qquad I-2-1$$

In this equation is:

Q_b the volumetric flowrate of the blood $\qquad$ ml/min
C_{bi} the inlet concentration of a solute in the blood $\quad$ g/l
C_{bo} the outlet concentration of a solute in the blood g/l
C_{di} the inlet concentration in the dialysate $\qquad$ g/l
Normally $C_{di}=0$ (except for some solutes as summarised in
table I-1), in which case the dialysance equals the clea-
rance, if a single pass dialysate flow is used:

$$Cl=\frac{(C_{bi}-C_{bo})}{C_{bi}}Q_b \qquad ml/min \qquad\qquad I-2-2$$

As can be seen from equation I-2-2 the clearance of an
artificial kidney for a particular metabolite is the hy-
pothetical volume of blood, which is totally cleaned from
that metabolite each minute.
Another way to describe the effect of a dialyser is by
means of the overall masstransfer coefficient K defined

by the equation:

$$\Phi_m = KA\Delta C_{log}$$
I-2-3

in which

Φ_m is the amount of metabolite removed from the
blood each second   kg/sec

K is the overall masstransfer coefficient   m/sec

A is the membrane surface area m^2

ΔC_{log} is the logarithmic averaged concentration
difference between blood and dialysate kg/m^3

The definition of ΔC_{log} depends on the apparatus used.
For a single pass cocurrent dialysate and blood stream it
is defined by

$$\Delta C_{log} = \frac{(C_{di}-C_{bi})-(C_{bo}-C_{do})}{\ln\frac{C_{bi}-C_{di}}{C_{bo}-C_{do}}}$$
I-2-4

The overall masstransfer coefficient depends on:

<u>1</u> the nature of the metabolite

<u>2</u> the thickness and the nature of the membrane

<u>3</u> the resistance for masstransfer in the blood and in the
dialysate.

It follows from the equations I-2-1 and I-2-2, that the
clearance and the dialysance depend on these parameters
and furthermore on the volumetric flowrate of the dialy-
sate and the blood.

The two approaches (the medical and the technological ap-
proach) of the dialyser generally use two different sys-
tems of units. Also in this thesis we will make use of
both systems of units with a preference of the practical
system (m, kg, sec) in the case of theoretical analyses.

I-3 The possiblities of an adsorption kidney

Two or three dialysis treatments in a week are necessary
for an uremic patient. Each treatment takes 8-12 hours and
is generally carried out in a hospital. It is obvious,

that the treatments are not only a physical inconvenience,
but also a mental stress for the patient.

A technical and medical team is necessary to assist the
treatment.

In the Netherlands the insurrance companies pay about f500
for each treatment, which amounts up to f50 million each
year for the thousand patients in this country.

Because of these facts it would be important if either the
number of treatments or the dialysis time could be reduced.
Homedialysis is an important improvement and the hemodia-
lyser with regeneration of a restricted quantity of dia-
lysate may facilitate this.

At the moment it is not possible to give a full alterna-
tive for the hemodialyser in order to decrease the number
of treatments or the duration of the treatment. A future
alternative might be the artificial kidney based on ad-
sorption. Such an artificial kidney removes the metaboli-
tes from the blood by means of adsorption (eg. activated
carbon), but also chemical reactions could assist for this
purpose. The blood of the patient may be flown through a
cartridge instead of through the dialyser. Such a cartrid-
ge could contain:

$\underline{a}$ activated carbon to remove all metabolites from the
blood except urea and ions

$\underline{b}$ an anion exchanger in the acetate form to exchange ace-
tate with Cl^-, $H_2PO_4^-$, HPO_4^{--} and PO_4^{---}

$\underline{c}$ a kation exchanger to exchange Ca^{++} for K^+, Na^+ and Mg^{++}

$\underline{d}$ urease to convert urea

$\underline{e}$ ionexchangers to adsorb the ammonium formed in step $\underline{d}$.

Because of this complicated composition the cartridge has
to be composed of different compartments. A direct contact
between the substances mentioned and the blood must also
be prevented as we will see in the following chapter.

Although such a cartridge becomes very complicated it has
several advantages:

$\underline{1}$ the system is smaller and more manageable than the dia-

lyser and home dialysis will be no problem anymore

2 the duration of the treatment will be shortened

3 no control is needed during the treatment

4 no dialysate container has to be used.

The disadvantages of the system are:

1 a rather high surface area (5-10 m^2) which increases the
amount of blood damage

2 a rather high priming blood volume is involved, which is
200-1000 cm^3 depending on the method of direct contact
preventing (see chapter II)

3 for the removal of water (to control the water balance
if needed) a ultrafiltration section has to be added as
well.

In order to decrease both the exchanging surface area and
the priming volume some of the functions of the cartridge
could be performed by medicaments.

In stead of aiming at a complete substitution of the dia-
lyser, one could also try a combination of the dialyser
and a less complete cartridge, based only on e.g. the
principle of adsorption at activated carbon in order to
reduce the costs and duration of the treatment.

During the last few years the symptoms of uremic patients
are ascribed more and more to the socalled middle molecu-
les (molecules with a molecular weight larger than 200)
and the small clearance of these molecules appears to be
the limiting factor in the dialysis treatment. These mid-
dle molecules are, however, good adsorbed by activated
carbon and thus an adsorber filled with carbon will be a
good supplement to the dialyser.

Besides for the use as an addition to the dialyser, such
an adsorber offers also possibilities for the removal of
exogenous poisons. In fact it appears to be very useful in
the removal of poisons in cases of autointoxications, but
also for patients with acute hepatitic failure.

The time needed for the removal of exogenous poisons by

means of adsorption is much less than either by means of
forced diuresis or by means of dialysis.
Other advantages of the adsorber above the dialyser are:
1 the direct applicability (e.g. in the ambulance)
2 the fact, that no disturbances are introduced in pH-
  and water balances, and in urea and ionic concentrations
3 the slight control needed during the treatment.

ARTIFICIAL KIDNEYS, WHICH MAKE USE OF THE PRINCIPLE OF
ADSORPTION

II-1 Review of litterature
II-1-a the adsorption by means of activated carbon

As is mentioned in paragraph I-3 activated carbon will
readily adsorb all metabolites from blood except urea and
ions, that are adsorbed to a lower extent and more slowly.
Although the adsorption mechanism of a solute from a so-
lution is not very well understood, it is generally as-
sumed, that the adsorption is caused by van der Waals for-
ces (C-5). The nonpolar adsorbent activated carbon will
therefore adsorb organic solutes with a molcular weight
larger than about 100 and ions with a high molecular
weight.
In previous studies (C-1 - C-8) it was found, that creati-
nine, uric acid and many other metabolites were readily
adsorbed on activated carbon.
Yatzidis (C-9) was the first, who used activated carbon in
direct contact with blood during hemoperfusion through a
cylinder. Afterwards Dunea (C-10) used the same type of
cylinder. Yatzidis and Dunea found, that creatinine, uric
acid and many other metabolites were adsorbed in contrast
with urea. Salicylates and barbiturates were also adsorbed
in this way. It appeared, however, that hemoperfusion over
activated carbon also introduced some disadvantages:
- a serious damage of the blood cells
- embolisms caused by release of small carbon particles
- adsorption of useful substances like proteins.

II-1-b dialysis with regeneration of the dialysate

To prevent the above mentioned disadvantages it is possible to make an indirect contact between the blood and the activated carbon particles.
One method is the dialysis with recirculation of the dialysate through a cylinder filled with carbon. This method was first proposed by Twiss and Paulssen (C-7).
Some years ago Gordon (D-1,2) introduced a more advanced method. He recirculated the dialysate over a cartridge containing:
1 activated carbon to adsorb all metabolites except urea
2 urease to convert urea into ammonia and carbon dioxide
3 ionexchangers (zirconium phosphate and zirconium oxide) to adsorb the liberated ammonia.
The advantage of such a dialyser is the small volume of dialysate, namely 2 litres, which makes homedialysis more feasible. The dialysis with recirculation of the dialysate has also some disadvantages:
1 the composition of the dialysate is not constant and the efficiency will be less for some compounds than with the use of normal dialysate.
2 the principle of dialysis is maintained and therewith the low clearance of the middle molecules. The duration and the costs of the dialysis treatment will therefore hardly be diminished.

II-1-c the microcapsule adsorber as artificial kidney

A second method to prevent direct contact between the blood and activated carbon is encapsulation of the carbon particles in semipermeable membranes (microcapsules). The blood is led through a cylinder containing these microcapsules.
This method is developed by Chang (E-1 - E-10) and afterwards also used by Andrade (E-13 - E-15). Chang encapsu-

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lated carbon particles with a diameter between 0,5 and 2
millimetres and he used collodion as coating material,
whereas Andrade used hydron. Besides Chang coated the mi-
crocapsules with albumen to prevent blood damage. Apart
from albumen coated collodion he also used heparin com-
plexed collodion as coating material. His microcapsule
artificial kidney is already clinically used for some
time (E-6). The microcapsule adsorber again has some dis-
advantages:

1 The risk of embolisms remains. A complete coating is
   very difficult to attain especially with smaller parti-
   cles and therefore a direct contact between blood and
   activated carbon is not entirely prevented. A washing
   procedure in order to remove small carbon particles,
   which are not encapsulated is therefore generally applied
   (see also E-15).
2 There is a high probability for channeling, especially
   along the cylinder wall, which causes an ineffective
   use of the adsorber.
3 It is impossible to use small carbon particles, because
   these are difficult to encapsulate and will furthermore
   cause a high pressuredrop over the adsorber. This has
   different consequences for the final apparatus: a small
   specific surface area, an overcapacity for adsorption
   and a large blood hold up (priming volume). This disad-
   vantage also holds for the dialyser with regeneration of
   the dialysate (see section II-1-b).

II-1-d the removal of urea

As is already mentioned an artificial kidney based on ad-
sorption at activated carbon hardly removes urea. At the
moment the best way to perform the removal of urea from
blood is the indirect one by hydrolysis of urea by means
of urease and adsorption of the produced NH_4^+ by ionex-
-changers. This system of urease and ionexchangers can be

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applied in three ways:

<u>1</u> The blood from a patient can be directed through a cylinder containing the mentioned compounds. Not only the carbon but also the urease and the ionexchangers must be prevented from direct contact with the blood.

<u>2</u> By oral ingestion of ionexchangers and urease. The ionexchangers may adsorb the NH_4^+ produced from urea by the bacteria in the gastrointestinal tract (F-3 - F-5). As the conversion of urea to NH_4^+ is rather slow, it might be necessary to ingest urease for the accelaration of the conversion. This oral ingestion is a addition to the hemoperfusion over carbon. In this way it is also possible to reach a constant urea concentration in the blood.

<u>3</u> The system urease - ionexchangers can be simplified by the adsorption of urease on the ionexchangers. We found (G-12), that urease was well adsorbed by means of HAHPV, which is a solid catalyst used in the oil industries for the cracking of heavy oils (see for further description appendix 1) and that this adsorption caused a higher activity of the urease. Moreover the produced NH_4^+ was adsorbed on the catalyst as well.
By the adsorption of urease at the ionexchanger the system urease - ionexchangers becomes smaller, than with a separate use of the components.
Since we concentrated on the film adsorber no further research was performed on this subject.

II-2 <u>The development of the film adsorber</u>

We passed the following stages during the development towards the final film adsorber:
<u>a the formation of a microcapsule adsorber</u>
According to the method of Chang we tried to make microcapsules. Much smaller carbon particles (40 μ) were used in order to obtain a large specific surface area. Good en-

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capsulation of these small particles, however, appeared to
be impossible. A high amount of particles was not encapsu-
lated at all, while most of the other particles were only
coated partly.

Another difficulty was, that a cylinder filled with these
small particles caused an enormous pressuredrop, which for
a cylinder (10 cm heigh and 5 cm in diameter) filled with
these particles will be of the order of 5,7 mH_2O, when
normal blood of 25^OC is led through the cylinder with a
volumetric flowrate of 100 ml/min. For blood of uremic pa-
tients at 37^OC this would be 3,2 mH_2O. We therefore choose
to search for an improved method.

b the production of chips

Thin sheets of collodion were made, in which the carbon
particles were embedded. The produced sheets were cut into
chips. In this way we obtained a good clearance for crea-
tinine with a cylinder filled with these chips.

While cutting these sheets, however, some carbon particles
were freed, which introduced again a direct contact be-
tween the blood and the carbon. The logical consequence
was to lessen the cutting by use of sheets.

c the use of sheets

Sheets of 10x5 cm were made with a thickness of 150 μ. A
pile of a hundred of these sheets was the active part of
the adsorber (10x5x2 cm).

The production of the sheets of a definite size still in-
troduced some cutting and consequently release of carbon
particles. All sheets must have the same breadth, because
otherwise a channeling is caused along the sides of the
pile. A short circuiting along the sides, however, could
not be prevented.

The last step was the production of a film in which no
cutting was needed.

d the production of a continuous film

The collodion film in which carbon particles are embedded
has a length of 10 m, a breadth of 10 cm and a thickness

of 150 μ. It is winded up to a roll, which is brought into
a cylinder. The blood is led axially through this roll. In
order to ensure, that a liquid film is maintained between
the consecutive windings of the roll, small glass beads
are embedded in the film together with the activated car-
bon. In a clinically used adsorber of this type the glass
beads will be replaced by beads of another kind of materi-
al (e.g. polystyrene or a poly acrylate), since glass
beads appear to cause an unallowable amount of blood damage.

II-3 Short description of the film adsorber

The film adsorber consists of the above described activa-
ted carbon collodion film (acc film), which is rolled up
on a trovidur core with a diameter of half a centimetre
and which is brought into a trovidur cylinder (see figure
II-1).

5 cm

10 cm
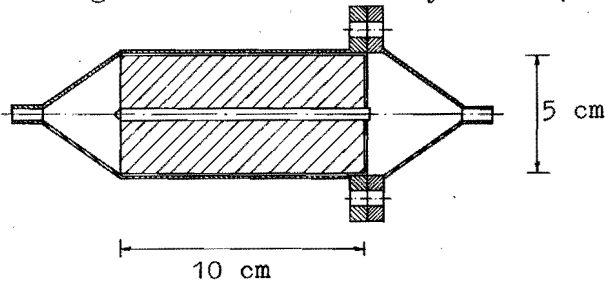
figure II-1 the film adsorber

In our experimental apparatus there is an inlet and an
outlet compartment of 20 ml each. In an ultimate design,
however, these compartments can without objection be re-
duced to only a few millilitres, since because of a rela-
tively high pressure drop over the film roll a good dis-
tribution of blood over the whole roll is ensured.
The composition of the film at operating conditions is:
water 66 %wt, activated carbon 21 %wt, collodion and glass
beads each 7 %wt. Some characteristics of the carbon are
given in appendix 1.
The glass beads, that are embedded in the film, have a

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diameter of 200-250 μ and spare a free space between the
windings of about 50 μ for the blood flow (see figure II-2).
As a consequence the blood hold up of the film adsorber is
50 ml, the exchanging surface area is 2 m^2 and the speci-
fic surface area is 100 cm^2/cm^3, while the exchanging sur-
face area of the microcapsule adsorber is only 15-40 cm^2
per cubic centimetres depending on the diameter of the
carbon granules.

The necessary volume of an adsorber depends on:

1 the adsorption capacity of the carbon

2 the masstransfer rate needed to adsorb a specific amount
  of solute in a specific time.

liquid
flow

acc film

glass beads
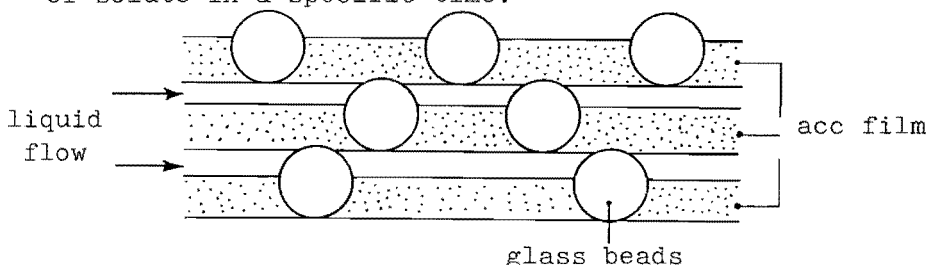
figure II-2 three windings of the acc roll

II-4 Description of the apparatus used to produce the film
II-4-a the original apparatus

In the original apparatus, that has been developed for the
preparation of the acc film (see figure II-3 and picture
II-1), a rotating drum or cylinder is partly immersed in a
tank T, that is filled with water. The cylinder is made of
brass and has a diameter of 65 cm and a wideness of 15 cm.
It is tightened around a bicycle rim B and centered by
means of spokes around the horizontal axis. The rotating
cylinder is driven by a motor M via a pulley and rotates
at about 1/6 cycle/minute.

A suspension of activated carbon in collodion (a 6 % solu-
tion of cellulose nitrate in ether and alcohol (4:1)) is
brought in a closed tray on top of the rotating cylinder.
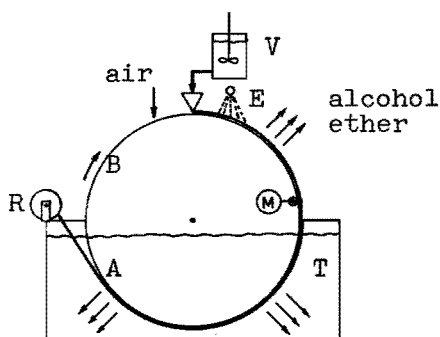
figure II-3 **the original apparatus**

The suspension is spread evenly over the wall of the cylin-
der through a slit at the bottom of the tray. The width of
the slit and the distance of the tray from the cylinder
wall can be varied. The suspension level in the tray is
kept constant by a regulated flow from a container V, in
which the suspension is continually stirred.
When the suspension has leaved the tray, it passes an ejec-
tor E, which sprays the glass beads on the film.
The ether is evaporated mainly from the film but the alco-
hol only sparingly. When the film reaches the water, the
larger part of the alcohol and most of the residue of the
ether is extracted.
Near A the film is drawn from the cylinder and whinched on
roll R. Finally the cylinder surface is blown dry before
returning to the spreading tray.
The production rate of the film is about 20 m/h.
It must be stressed, that the film produced in this way
should not be dried, since drying causes an irreversible
shrinking and brittleness of the film.
Roll R may contain up to about 150 m of film. Since the
rolls in the film adsorber contain only 10 m of film a re-
winding mechanism is necessary. During this rewinding care
is taken, that no air is introduced and that the space be-
tween the windings is entirely filled up with water. The
rewinding is therefore carried out underneath the water.
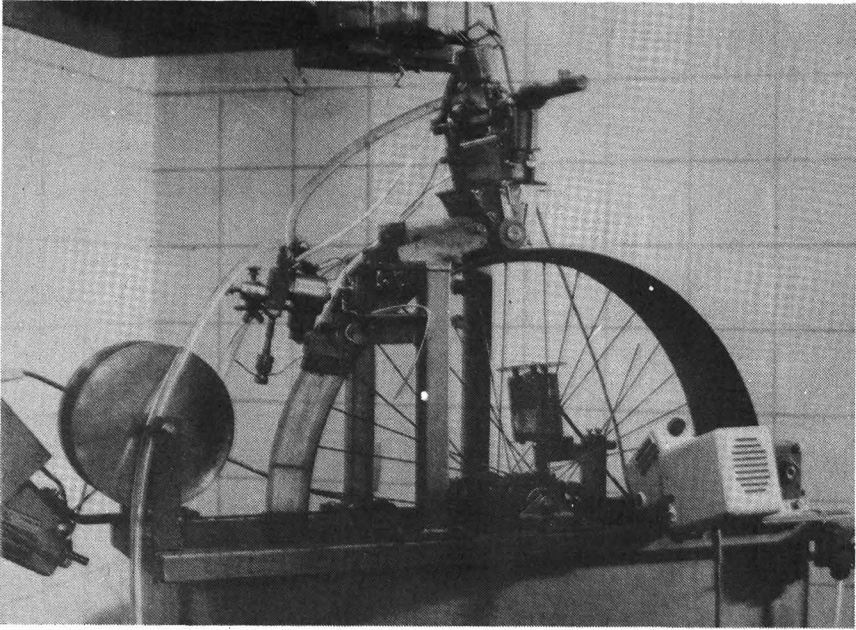
picture II-1 <u>the original apparatus</u>
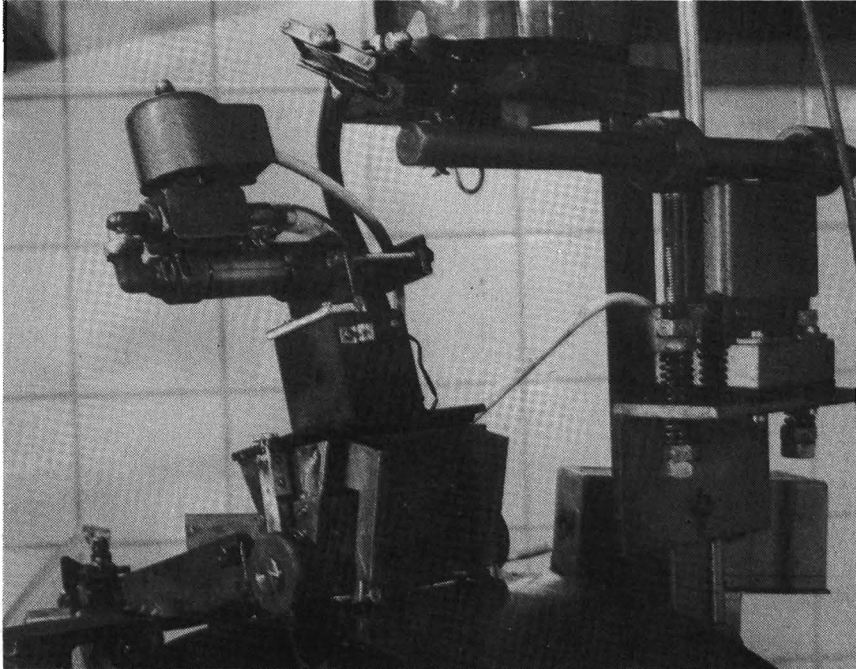
picture II-2 <u>the spreading tray and the level controller</u>

Before the adsorber is used, it is rinsed for the removal
of the residues of ether and alcohol with about 20 l of
water. Besides, for tests with blood, the adsorber is equi-
librated with 5 l of a saline solution (9 g NaCl per litre).

II-4-b the spreading tray and the level controller

A sketch of the spreading tray and the level controller is
given in figure II-4a and 4b and in picture II-2. The
spreading tray is made of brass and is triangular in cross
section. One side Z can be moved by means of adjusting
screws M_s, sothat the width of the slit S is variable be-
tween 0 and 0,5 mm. Experimentally was found, that 0,2 mm
gives the best results at a rotation of 1/6 cycles/minute.
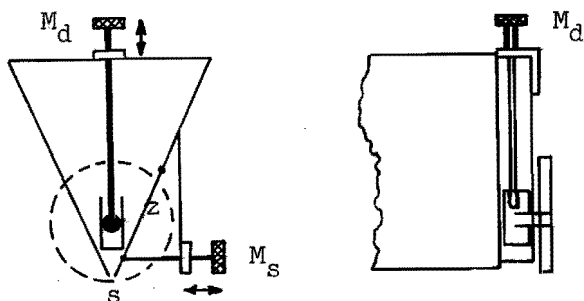
figure II-4a the spreading tray

The distance between the tray and the cylinder can be
varied as well by means of screws M_d, which are connected
with the weels, on which the spreading tray moves on the
rotating cylinder.
A float F is placed upon the acc suspension in the spread-
ing tray. This float blocks the light from a light source
L to the light sensible cell C. When the level of the sus-
pension sinks the light way is unblocked and by way of a
relais R a magnetic valve V is closed. This serves a pres-
sure cylinder P to open a tube B, which connects the
spreading tray with container V.

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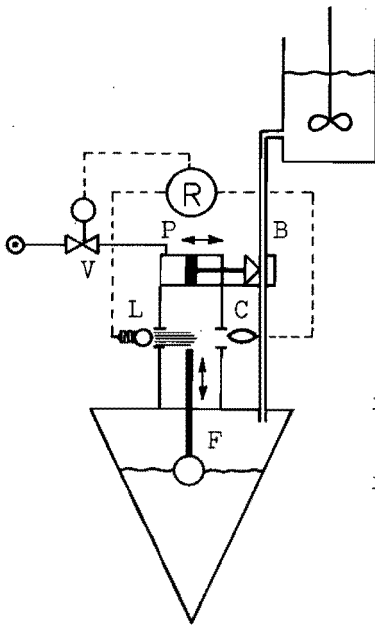
figure II-4b the spreading tray and
the level controller
figure II-5 the improved type of
apparatus
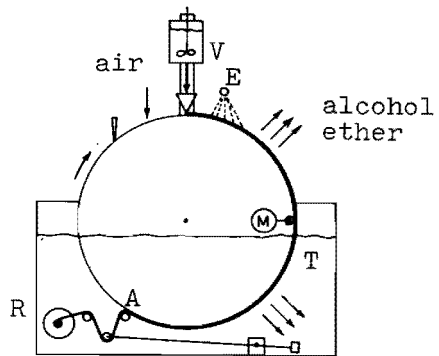
II-4-c the improved type of apparatus

With the original type of apparatus all the film adsorbers
are prepared, that are used for the experiments described
in the following chapters (except for the experiments des-
cribed in paragraph IV-7; the adsorbers used there were
prepared with the improved apparatus). This improved type
(see figure II-5 and picture II-3) is developed with the
know how obtained with the original apparatus.
It operates fully automatically. The films, produced by
means of this apparatus, have a more constant thickness
and are more easily released from the rotating drum.
As in the original type a rotating drum is partly immersed
in a tank with water. The drum consists of a chromium pla-
ted cylinder (65 cm in diameter and 40 cm wide), which is
tightened around three circular brass plates. The cylinder
is wider than that of the original type, so that there are
more possibilities concerning number and breadth of the
produced films. This is done in view of the different

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picture II-4 <u>the sprea-</u>
<u>ding tray, the ejector,</u>
<u>the level controller</u>
<u>and the container</u>
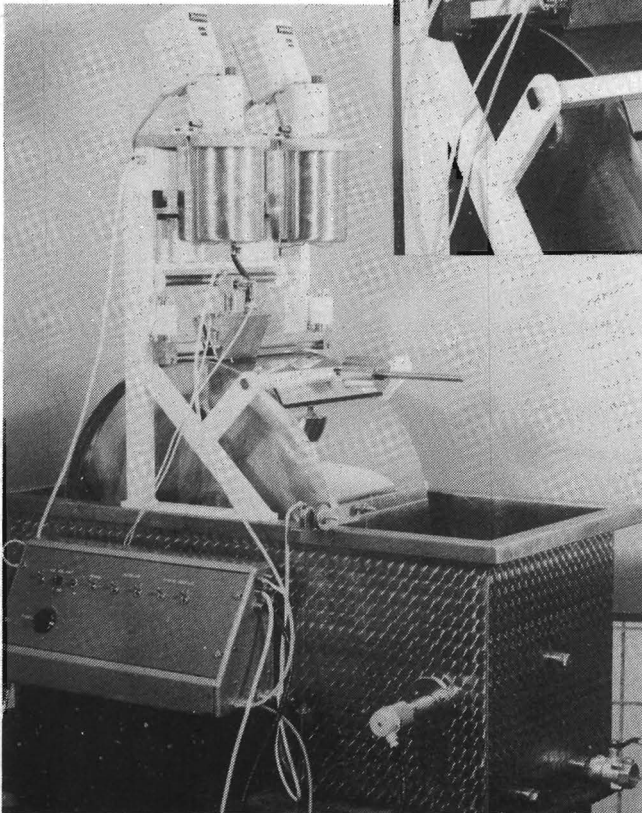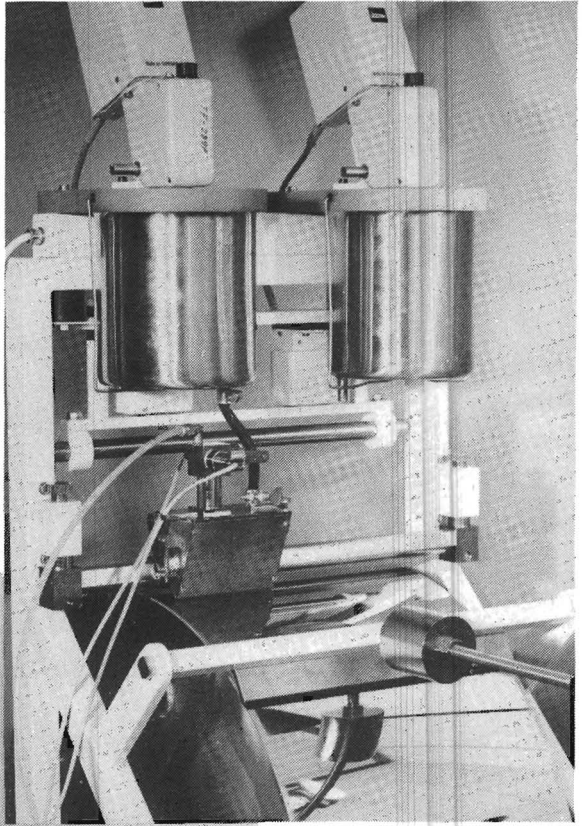
picture II-3 <u>the</u>
<u>improved appara-</u>
<u>tus</u>

kinds of application as mentioned in paragraph I-3. The
spreading tray has a constant slit of 0,2 mm, but the dis-
tance between the tray and the drum is still variable.
The suspension level controller and the ejector of the
glass beads are of the same design as in the original
type.
The whinching on the roll is performed underneath the wa-
ter to avoid the introduction of air between the windings
of the roll. The force, with which the film is whinched
is automatically regulated. This facilitates the rewin-
ding and improves the reproducebility. In picture II-4
the spreading tray, the ejector, the level controller and
the container are shown.

II-5 Costs evaluation of the film adsorber

starting points
We would need 2000 adsorbers in a week or 100000 in a year
starting from an estimation of 1000 patients in the Nether-
lands. One film production apparatus produces 4 adsorbers
in one hour, because it has two tracks each with a film
production rate of 20 m/h as we have used. This rate may
be raised. The working schedule is 5 days à 8 hours a week.
The production of one apparatus is therefore 160 adsorbers
a week. 15 apparatus (2 reserve) would be needed to fulfil
the requirements of the Netherlands. These apparatus can
be operated by 15 men. Furthermore 3 men for additional
activities like sterilisation and filling of the cylinders
would be needed as well as a supervisor.

investments
film apparatus   f375000
other equipment f300000
building   f400000
                 f1075000

the materials needed for one adsorber

30 g carbon	à f10/kg	f0,30
180 g collodion	à f5 /kg	f0,90
15 ml alcohol	à f10/l	f0,15
60 ml ether	à f10/l	f0,60
10 g glass beads	à f20/l	f0,20
cylinder	à	f0,25
		f2,40

Costs in one year

depreciation (in three years) and capital costs	f500000
salaries (nine men)	f270000
costs of materials	f240000
overhead	f100000
research	f100000
sale expenses	f100000
utilities	f100000
	f1410000

The production costs of one adsorber therefore are estimated to be f14,10

C H A P T E R   III

THE TECHNOLOGICAL ANALYSIS OF THE FILM ADSORBER

Since the medical requirements demanded from the film ad-
sorber are given, one can also deduce the technological
standards, which have to be satisfied. A satisfactory o-
peration will depend on:
<u>a</u> the flow distribution through the adsorber
<u>b</u> the adsorption capacity
<u>c</u> the masstransfer and the adsorption rate.
The flow distribution is studied in paragraph III-1.
In paragraph III-2 some experiments are described, which
are related to the different masstransfer mechanisms in
the adsorber and the adsorption rate. The measurement of
the adsorption isotherms is also described in this para-
graph. The result of these experiments can be integrated
into a model describing the functioning of the adsorber.
This is done in paragraph III-3.

III-1 <u>The flow phenomena in the film adsorber</u>

The ideal flow corresponds with what is generally called
plug flow, which means, that any liquid element has the
same residence time in the adsorber. Two extreme depar-
tures, which might occur are:
- dead corners, where the liquid does not flow at all
- short circuits, through which the liquid passes very
  fast; no proper adsorption from this liquid is possible.
There are however many intermediate flow patterns such as
that caused by a spread in the liquid film thickness. In
section III-1-a the residence time distribution is mea-
sured, which gives an idea of the flow distribution. This
residence time distribution is also theoretical treated
by means of the criterium of Taylor. From the mean resi-
dence time a mean liquid film thickness can be calculated.

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In section III-1-b the relation between the pressuredrop and the liquid velocity of a Newtonian liquid is used to measure a mean liquid film thickness as well.
In section III-1-c these two methods are compared with the direct measurement of the liquid film thickness.
In the last section (III-1-d) of this paragraph the relation between the pressuredrop and the velocity is measured, while the adsorber is flown through by bovine blood. The result is compared with some models on the rheology of blood.

III-1-a the residence time distribution in the film adsorber

We used albumen as a tracer for the measurement of the residence time distribution (RTD). This compound does not penetrate in the acc film. The small adsorption at the collodion surface (see chapter IV) does influence the measurement, as will be proven in section III-1-c, but the influence is only small.
By means of a hypodermic syringe a pulse injection of 1,5 cm^3 albumen solution (6,5 g/l) was given at the inlet of the adsorber, while the adsorber was flown by a saline solution with a volumetric flowrate of 30 cm^3/min. Continually samples were drawn of 10 cm^3 (which took 20 sec) at the outlet of the adsorber alternated with 20 seconds during which no samples were drawn.
Under the same conditions another experiment was performed in which a similar injection was given. Again samples were drawn alternating with 20 seconds without sampling, but now with a time shift of 20 seconds as compared to the first experiment.
The albumen concentration in the samples was measured and the result is given in table III-1 (under column C_1 for the first experiment and under column C_2 for the second one). With the obtained concentrations a cumulative curve

was composed, which is given in graph III-1. Curve a of
graph III-2 shows the output concentration of the adsorber
as calculated from graph III-1: $C_o = dF/dt$. This is the re-
sidence time distribution curve.
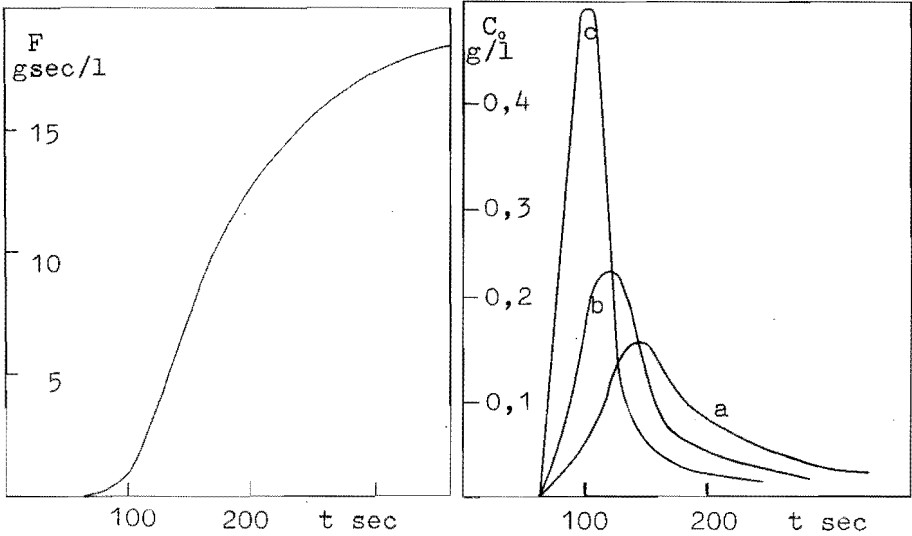
graph III-1 the cumulative residence time distribu-
            tion curve
graph III-2 the residence time distribution curve
            a: no correction applied; b: correc-
            ted for one compartment; c: corrected
            for two compartments

The two compartments before and after the roll behave as
ideal mixers, as is concluded after injections with a dye
before the adsorber as described in section II-2-c. This
adsorber was transparant and had also two compartments like
the film adsorber. The dye injections showed, that no pre-
ferential streamlines appeared in the compartments. The
course of the concentration was comparable to the course
in an ideal mixer.
The RTD as shown in curve a of graph III-2 is therefore

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composed of the RTD curves of the roll and of the two com-
partments. The RTD of the roll can now be calculated from
curve a by means of the procedure indicated in appendix 3.
The result of this calculation is given in table III-2 and
graph III-2 (curve c).
In graph III-3 this corrected RTD curve is compared with
the RTD curve of a Poiseuille flow through a slit between
two parallel planes, where there is no radial diffusion.
This last distribution is given by the formula which is
shown in this graph as well.
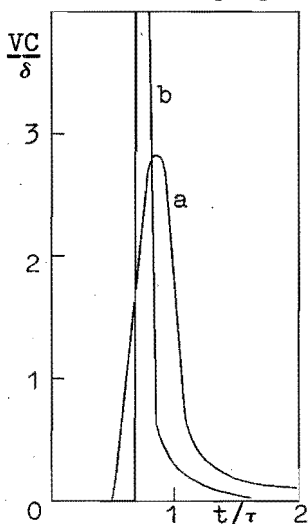
curve a measured and corrected
curve b calculated by means of

$$\frac{VC}{\delta} = \frac{1}{6(t/\tau)^3} \cdot \frac{1}{\sqrt{1-2/3(t/\tau)}}$$

graph III-3 <u>the residence time
distribution</u>

The deviations between these two curves might be explained
by the occurence of radial diffusion, but also by a spread
in the film thickness.
Graph III-4 gives RTD curves measured with KCl. Since KCl
can easily penetrate in the acc film and in the carbon
particles its mean residence time is much higher. The KCl
concentration was measured conductometrically. The RTD
curve of KCl seems more to be like the RTD curve of an ap-
paratus with a plug flow and axial mixing. Some tailing is
showing because of the lag caused by the diffusion in the
film and the carbon particles.

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table III-1 <u>the residence time distribution of albumen</u>
<u>(no correction applied for the compartments)</u>

t	C_1	C_2	$C_1\Delta t$	$C_2\Delta t$	F	$tC_1\Delta t$	$tC_2\Delta t$	dF/dt
80	0,010		0,20		0,20	14		0,024
100		0,040		0,80	1,00		72	0,063
120	0,104		2,08		3,08	228		0,122
140		0,136		2,72	5,80		353	0,154
160	0,156		3,12		8,92	468		0,127
180		0,107		2,14	11,06		364	0,093
200	0,082		1,64		12,70	312		0,076
220		0,068		1,36	14,06		285	0,0625
240	0,057		1,14		15,20	262		0,0509
260		0,044		0,88	16,08		219	0,0400
280	0,033		0,66		16,74	178		0,0320
300		0,030		0,60	17,34		173	0,0272
320	0,021		0,42		17,76	130		0,0186
340		0,019		0,38	18,14		125	0,0166
360	0,014		0,28		18,42	98		0,0095
380		0,012		0,25	18,67		92	
400	0,011		0,23		18,90	89		
420		0,007		0,14	19,04		57	
440	0,006		0,12		19,16	51		
460		0,005		0,11	19,27		49	
480	0,005		0,11		19,38	52		
500		0,005		0,11	19,49		54	
520	0,005		0,10		19,59	51		
540		0,004		0,08	19,67		42	
560	0,004		0,08		19,75	44		
580		0,004		0,07	19,82		40	
600	0,002		0,03		19,85	17		
620		0,002		0,03	19,88		17	
640	0,001		0,02		19,90	12		
660		0,001		0,01	19,91		6	

table III-1 (continued)

C_1 and C_2 are the output concentrations of the first and
the second experiment (g/l)

$F=\Sigma C_1 \Delta t + \Sigma C_2 \Delta t$ (gsec/l)

the total amount of albumen in the output of the
adsorber was 9,95 mg, while 9,75 mg was injected

$\Sigma t C_1 \Delta t + \Sigma t C_2 \Delta t = 3954$

the mean residence time of the adsorber was
3954/19,91. the mean residence time of the roll
was 118 sec

$C_o = dF/dt$ the real output concentration of the film adsor-
ber

table III-1 the correction of the residence time distribu-
tion for the two compartments

t	dF/dt	C_{c1}	C_{c2}	VC_{c2}/δ	t/τ	VC_{c2}^{cal}/δ
80	0,024	0,073	0,290	1,71	0,68	19,3
100	0,063	0,204	0,494	2,92	0,85	0,62
120	0,222	0,227	0,227	1,33	1,02	0,264
140	0,154	0,154	0,068	0,40	1,19	0,150
160	0,127	0,073	0,041	0,24	1,36	0,095
180	0,093	0,053	0,029	0,17	1,53	
200	0,076	0,046	0,023	0,14	1,69	
220	0,062	0,036	0,020	0,12	1,87	
240	0,051	0,031	0,017	0,10	2,03	
260	0,040	0,020	0,008	0,05	2,20	
280	0,032	0,017	0,008	0,05	2,37	
300	0,022	0,014	0,006	0,04	2,54	

C_{c1} and C_{c2} are the output concentrations after correction
for respectively one and two compartments (g/l);
δ is the amount of albumen injected (g); V is the priming
volume (l); τ is the mean residence time (sec).

The difference between the RTD curves of albumen and KCl
is in agreement with the criterium of Taylor (H-1). Star-
ting from the convective diffusion equation Taylor (see
also Levich (H-25)) derived a criterium stating, when a
Poisseuille flow should be treated like a plug flow with
axial diffusion. He derived this criterium for a flow
through a circular pipe. In appendix 5 we derived a simi-
lar criterium for a flow through a slit. The result is:

$$LD/\bar{v}d_1^2 \gg 10 \hspace{4cm} III-1-1$$

If this criterium fits, the flow should be treated like a
plug flow with axial diffusion.
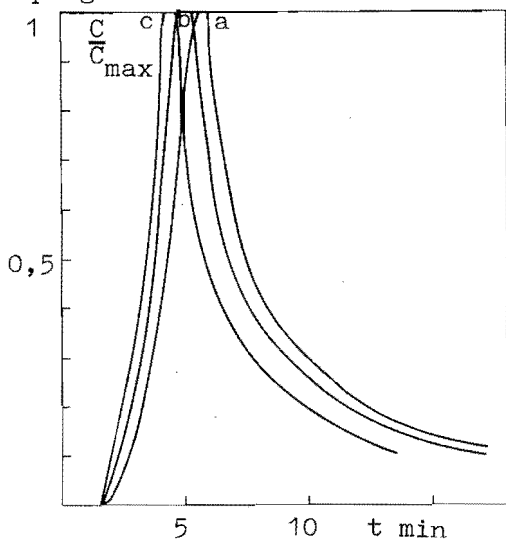
curve a no correction ap-
         plied
curve b corrected for one
         compartment
curve c corrected for two
         compartments

graph III-4 <u>the residence
time distribution of KCl</u>

For albumen (D=0,07.10^{-9} m^2/sec) LD/$\bar{v}d_1^2$=3 and no plugflow
should be expected.
For KCl (D=2.10^{-9} m^2/sec) LD/$\bar{v}d_1^2$=100 and in this case a
plug flow with axial mixing should be expected, although
the criterium does not take the diffusion in the acc film
into account.
Futher on in this chapter some experiments with creatini-
ne are described. For this compound holds LD/$\bar{v}d_1^2$=32 if
Q=30 ml/min.
In table III-1 the mean residence time is calculated from

the RTD curve of albumin. After correction for the resi-
dence time in the two compartments its value is 118 sec.
The liquid hold up (priming volume) is therefore 59 cm^3
and the distance between the windings is 52,2 μm.

III-1-b the pressuredrop over the film adsorber

The room between the windings of the roll can be conside-
red as a very broad slit and the pressure drop for a New-
tonian fluid over a slit is described by the following e-
quation:

$$\Delta p = \frac{12 Q \eta L}{d_1^3 b} \qquad\qquad III-1-2$$

in which

Δp is the pressuredrop over the film adsorber

Q is the volumetric flowrate

η is the viscosity

L is the length of the liquid to flow (breadth of the
   roll)

d_1 is the thickness of the liquid film

b is the breadth of the slit (length of the roll)

The next pressuredrops were measured when the film adsor-
ber was flown by water:

$Q = 30$ cm^3/min $\Delta p = 392$ N/m^2

$Q = 48$ cm^3/min $\Delta p = 657$ N/m^2

From equation III-1-2 the thickness of the liquid film ap-
pears to be respectively 47,6 μm and 46,7 μm. The corres-
ponding liquid hold ups are 52,7 cm^3 and 51,5 cm^3.

III-1-c conclusions

An arbitrary winding of the roll has a outer circumference

$$2\pi(r_o + px) \qquad\qquad III-1-3$$

in which

r_o is the radius of the core on which the film is rolled

p   is the number of the arbitrary winding counted from the
     core
x   is the thickness of the winding (the sum of the thick-
     ness of the acc film and the liquid film)

The sum of the lengths of all the windings of the roll
equals the length of the film

$$b=\sum_{p=1}^{p=n} 2\pi(r_o+px) \qquad\qquad\qquad \text{III-1-4}$$

in which
b is the length of the film
n is the number of windings of the roll
Equation III-1-4 is an arithmetic progression, of which
the sum is given by:

$$b=2\pi r_o n+\tfrac{1}{2}n(n+1)2\pi x \qquad\qquad \text{III-1-5}$$

For the last winding applies

$$2\pi R=2\pi(r_o+nx) \qquad\qquad\qquad \text{III-1-6}$$

in which R is the inner radius of the cylinder containing
the roll. Elimination of n from equation III-1-6 and
III-1-5 renders:

$$x=\frac{\pi(R^2-r_o^2)}{b-(R-r_o)} \qquad\qquad\qquad \text{III-1-7}$$

For the dimensions of the film adsorber, which we used in
our experiments, applies R=2,5 cm and r_o=0,5 cm.
The thickness of the collodion film d_f can be measured
with a micrometer. The liquid film thickness d_l equals
$(x-d_f)$. In the film adsorber we used for the measurements
in this paragraph d_f=118 μm (which result was found by
means of 52 measurements with a relative standard devia-
tion of 6%) and b=1129. x was calculated to be 166 μm. The
mean liquid film thickness is therefore 48 μm and the cor-
responding liquid hold up is 54,2 cm^3.
We have now used three methods to measure the liquid film
thickness. The results of these measurements are

measurement	film thickness	hold up
RTD	52,2 μm	59 cm^3
pressuredrop	47,6	52,7
	46,7	51,5
direct	48,0	54,2

Since the result of these measurements corresponds supri-
singly well, it can be concluded, that the flow pattern
through the adsorber satisfies a high standard and that
no dead corners or short circuits of significance are
present. Also in section III-1-d a good example of the
good similarity of the values of direct geometrical mea-
surement and the pressuredrop values is given.
The values found by the RTD measurement are slightly
higher. This is probably caused by the adsorption of al-
bumen at the collodion surface. From graph IV-2 it follows
that from an albumen solution (0,5 g/l), which is led
through the film adsorber with a volumetric flowrate of
30 ml/min 0,06 g is adsorbed in 20 minutes. When we look
at curve b of graph III-2, which gives the concentration
at the output of the roll, it seems justified to say, that
the roll is flown during 20 seconds by an albumen solution
with a concentration of 0,1 g/l. During the RTD measure-
ment about 0,0012 g will be adsorbed out of the original
0,01 g, that was injected. The rate of desorption, however
is unknown, but since all albumen left the adsorber in
less than 600 seconds it seems justified to say, that the
influence of the adsorption is only small. The measurement
of the liquid hold up, however, can be better performed by
means of the measurement of the relation between the pres-
sure drop and the velocity.

III-1-d the rheological behaviour of blood in the film
         adsorber
III-1-d1 the measurement of the pressuredrop

For this experiment the set up shown in figure IV-1 was
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used. The pressuredrop was measured with a differential
pressure indicator, existing of a half filled inverted U-
tube.
In the first experiment an adsorber was first flown by wa-
ter of 25°C and afterwards by bovine blood of 25°C. In
both cases the pressuredrop over the film adsorber was
measured at different volumetric flowrates.
In another experiment a film adsorber was first flown by
bovine blood of 37°C and afterwards by water of 37°C. The-
se two experiments were performed in order to control if a
possible clotting has influence on the measurement.
The result of the measurement is shown in graph III-5 .
The result of the measurements with water is given toge-
ther with other data concerning the two adsorbers in ta-
ble III-3.
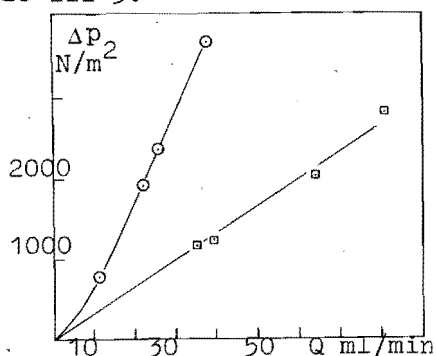
o adsorber 1

□ adsorber 2

graph III-5 <u>the pressuredrop</u>
<u>measurement when the adsorber</u>
<u>is flown by bovine blood</u>

III-1-d2 <u>the theoretical explanation of the pressuredrop</u>

Blood is a suspension of blood cells in plasma. The volume
percentage of blood cells is usually called hematocrit.
For healthy men this hematocrit is 40-50 and for uremic
patients about 20.
As blood is a suspension, it may be considered as a so cal-
led Cassonian fluid, for which Casson (I-1) defined the
following relation:

$$\tau^{\frac{1}{2}} = \tau_0^{\frac{1}{2}} + \eta_s^{\frac{1}{2}} \nu^{\frac{1}{2}} \qquad \qquad III-1-8$$

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in which

τ	is the shear stress	N/m^2
τ_o	is the yield value	N/m^2
γ	is the shear rate	sec^{-1}
η_s	is the cassonian viscosity	$Nsec/m^2$

By means of equation III-1-8 one can calculate the pressure drop over the film adsorber as a function of blood velocity. This is done in section III-1-d2a. To this simple model one can add two refinements as is done in the sections III-1-d2b and III-1-d2c.

III-1-d2a the Casson model

By means of equation III-1-8 the following relation between the pressure drop and the velocity for a flow of a suspension between two parallel planes can be derived:

$$3\eta_s\bar{v}/a\tau_o = \tau_D - 12\tau_D^{\frac{1}{2}}/5 + 3/2 - \tau_D^{-2}/10 \qquad \text{III-1-9}$$

in which
2a is the distance between the planes
L is the length of the planes
Δp is the pressure drop
$\bar{v}$ is the mean velocity
$\tau_D = a\Delta p/\tau_o L$

This equation is derived by Merill (I-7) and Kooyman (I-5). In the graphs III-6a and 6b curve a shows τ_D as a function of the dimensionless velocity $3\bar{v}\eta_s/a\tau_o$, as it is given by equation III-1-9. For the application of this equation to our experiments the following parameters have to be estimated:
- the viscosity (η_s)
The formula most used for the calculation of the viscosity is the formula of Einstein

$$\eta_s = \eta_p/(1-\alpha\varphi) \qquad \text{III-1-10}$$

in which

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η_s is the viscosity of the serum
η_p is the viscosity of the plasma
φ is the volume fraction of blood cells
α Charm and Kurland (I-4) have found that

$$\alpha = 0{,}076\exp\{2{,}49\,\varphi + \frac{1107}{T}\exp(-1{,}690)\} \qquad \text{III-1-11}$$

in which T is the temperature (^{O}K).
A second formula for the viscosity is given by Kooyman:

$$\eta_s = \eta_p\exp2{,}05\varphi \qquad \text{III-1-12}$$

For the calculation of η_p another formula of Kooyman may
be used

$$\eta_p = 0{,}00135\exp2{,}78(1000/T-1000/310) \qquad \text{III-1-13}$$

- the yield value (τ_o)
In the litterature a lot of different values are proposed
for the yield value (I-2 - I-4). As seen from equation
III-1-9 the value of τ_o does not influence the relation
between pressure drop and mean velocity a great deal.
For our calculations we used the values of τ_o as given by
Kooyman (I-5) as these values are about the average of the
values as found by others (see for comparison Kooyman) and
agree with the value as found by Cokelet (I-2).
The relation of Kooyman is

$$\tau_o = (0{,}08 + 0{,}35\varphi)^3 \qquad \text{III-1-14}$$

- the volume fraction of blood cells (φ)
The hematocrit of the blood, that we used is about 50.
With this value the yield value and the two different vis-
cosities can be calculated respectively by the equations
III-1-14, III-1-10 and III-1-12.
Since the difference between the two calculated viscosities
is only small (<5%) we used the mean value.
With the resulting values a relation between the pressure
drop and the blood velocity can be calculated for our ex-
periments. The relation between τ_D and the dimensionless
velocity is shown in graph III-6a and graph III-6b (curve
b) for the first and the second experiment respectively.

Since the agreement with the theoretical curve (curve a of graph III-6a and 6b) is rather poor, we applied a refinement to the Casson model.
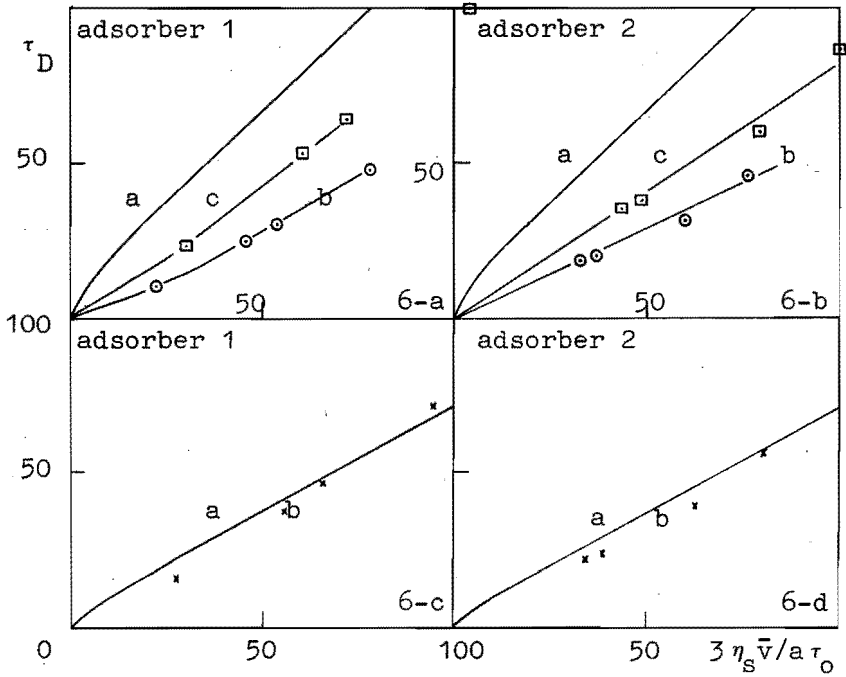
graph III-6 the theoretical explanation for the pressuredrop measurement

III-1-d2b the first refinement to the Casson model

When blood flows from a container through a channel with a small diameter (below 3.10^{-4} m) the mean hematocrit in the channel is smaller than the hematocrit in the container as was first observed by Fahreus in 1929. This is a consequence of the fact, that the hematocrit in the channel is a function of the place in the channel.
The relative hematocrit (quotient of the hematocrit in the channel and the hematocrit in the reservoir) is measured by Barbee and Cokelet (I-6) as a function of the hemato-

crit in the reservoir and the diameter of the channel. In
graph III-7 the relative hematocrit is given as a function
of the diameter of the channel (the hematocrit in the re-
servoir is 50). By means of this graph the hematocrit in a
channel can be calculated.
We applied this graph also for a slit and then new values
can be calculated for the yield value and the viscosities
of the blood. Also a new relation between τ_D and the di-
mensionless velocity is obtained. This is shown as curve c
in the graphs III-6a and 6b respectively for the first and
the second experiment.
Although the agreement with the theoretical relation is
better than with the pure Casson model, it is still unsa-
tisfactory. We therefore applied a second refinement.
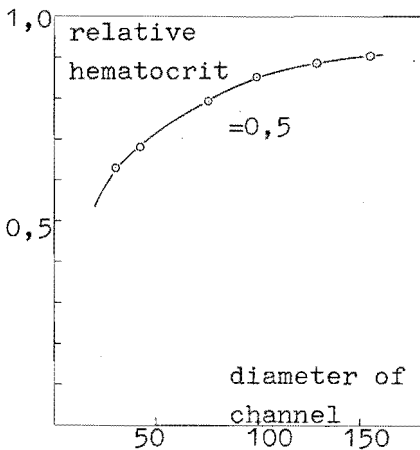
graph III-7 <u>the hematocrit in a</u>
<u>small channel</u>

III-1-d2c <u>the second refinement to the Casson model</u>

Since the hematocrit is a function of the place in the
channel, the flow pattern will be different from the flow
pattern as calculated from the Casson relation (equation
III-1-8). As a model one may assume a marginal plasma lay-
er. Charm (I-7) has measured the thickness of such a layer
as a function of the channel diameter and the hematocrit.
Assuming a marginal plasma layer Charm and Kurland (I-4)
derived a velocity pressuredrop relation in the same way

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as is done for equation III-1-9 for a capillar. We did
the same for a flow between two parallel planes (see ap-
pendix 6) and the result was:

$$3 \eta_s \bar{v}/a \tau_o = \tau_D[(1-\Delta^3)/(1-\alpha\varphi) + \Delta^3] -$$
$$- 12\Delta^{3/2} \tau_D^{\frac{1}{2}}/5 + \tfrac{1}{2}\Delta^2 \qquad\qquad III-1-15$$

in which $\Delta = 1-2\delta/a$ and δ is the thickness of the plasma
layer. δ will be about 5μ as can be concluded from the
measurements of Charm and Kurland.
α, φ and Δ can now be calculated and also the relation be-
tween the pressure drop and the velocity.
The curves a of the graphs III-6c and 6d represent a plot
of τ_D against the dimensionless velocity following equa-
tion III-1-15 for the two experiments, whereas the points
b of these graphs represent the measurement. A good agree-
ment between the theoretical and the measured curves is
obtained.
In table III-3 different data for the two adsorbers are gi-
ven as well as the result of the different calculations.

table III-3 <u>the pressure drop over the film adsorber when</u>
<u>it is flown by bovine blood</u>

<u>adsorber 1</u>   <u>adsorber 2</u>

<u>a the measurement with water</u>

$T=298°K$ $\eta_p=1,88$ cp $T=310°K$ $\eta_p=1,35$ cp
$d_1=41$ $L=9,6$ cm $b=950$ cm $d_1=50$ $L=9,7$cm $b=9,8$ m

Q ml/min	Δp N/m^2 measured	Δp N/m^2 calcu- lated	Q ml/min	Δp N/m^2 measured	Δp N/m^2 calcu- lated
30	626	656	21	245	256
			79	970	990

b the measurement with bovine blood

Q ml/min	Δp N/m^2	Q ml/min	Δp N/m^2
11	840	35	1140
22	1920	39	1260
26	2360	64	2010
38	3670	81	2900

c the Casson model

$$\varphi = 0,5 \quad \tau_o = 0,016 \text{ N/m}^2$$

$\alpha=1,31$	$\eta_s=5,30$		$\alpha=1,23$	$\eta_s=3,76$ cp	
Q ml/min	τ_D N/m^2	$3\eta_s\bar{v}/a\tau_o$	Q ml/min	τ_D N/m^2	$3\eta_s\bar{v}/a\tau_o$
11	11,2	22,7	35	18,4	32,9
22	25,6	45,4	39	20,3	36,7
26	31,5	53,6	64	32,4	60,2
38	49,0	78,4	81	46,8	76,2

d application of the relative hematocrit

$\varphi=0,337 \quad \tau_o=0,0077$ N/m^2 $\varphi=0,357 \quad \tau_o=0,0086$ N/m^2

$\alpha=1,44 \quad \eta_s=3,68$ cp $\alpha=1,30 \quad \eta_s=2,62$ cp

Q ml/min	τ_D N/m^2	$3\eta_s\bar{v}/a\tau_o$	Q ml/min	τ_D N/m^2	$3\eta_s\bar{v}/a\tau_o$
11	23,3	30	35	34,3	43,6
22	53,3	60	39	37,8	48,6
26	65,5	71	64	60,2	79,6
38	101	104	81	87	101

e application of the marginal plasma layer

$\delta=3,8\mu \quad \Delta=0,82 \quad \varphi=0,411$ $\delta=5,0\mu \quad \Delta=0,8 \quad \varphi=0,445$

$\tau_o=0,011$ N/m^2 $\alpha=1,37$ $\tau_o=0,0132$ N/m^2 $\alpha=1,29$

$\eta_s=4,32$ cp $\eta_s=3,19$ cp

Q ml/min	τ_D N/m^2	$3\eta_s\bar{v}/a\tau_o$	Q ml/min	τ_D N/m^2	$3\eta_s\bar{v}/a\tau_o$
11	16,7	27,3	35	22,2	34,5
22	38,1	54,6	39	24,5	38,5
26	46,8	64,6	64	39,2	63,2
38	73	94,4	81	56,5	80

III-2 The masstransfer mechanisms in the film adsorber

A model describing the functioning of the film adsorber
needs to integrate the adsorption isotherms (see section
III-2-a) and the following masstransfer mechanisms (see
also figure III-3):
- the diffusion in the liquid film (section III-2-b)
- the masstransfer from the liquid film (see section
  III-2-c)
- the diffusion in the acc film (see section III-2-d)
- the masstransfer in the carbon particles (see section
  III-2-e).

III-2-a adsorption isotherms

To get an idea of the capacity of the film adsorber ad-
sorption isotherms were measured for creatinine, inulin
and bromphthalein. An adsorption isotherm is the relation
at constant temperature between the adsorbed quantity of
a certain compound and the concentration of that compound
in the liquid at equilibrium.
For the measurement of the adsorption isotherms solutions
were made for the particular compound, after which a cer-
tain amount of activated carbon (not encapsulated) was
added to the solution. For all experiments mentioned in
this thesis "Merck" activated carbon was used (see appen-
dix 1 for further description).
The thus obtained suspension was shaken for such a long
time, that we could assume, that adsorption equilibrium
was reached and then filtrated. The concentration of the
compound in the filtrate was measured (see appendix 2 for
all quantitative analyses). For creatinine the adsorption
equilibrium is reached within 10 minutes (see graph III-12).
In graph III-8a the adsorption isotherms of the compounds
mentioned are given. In graph III-8b the adsorption iso-
therm of creatinine is given separately too.

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graph III-8a adsorption isotherms
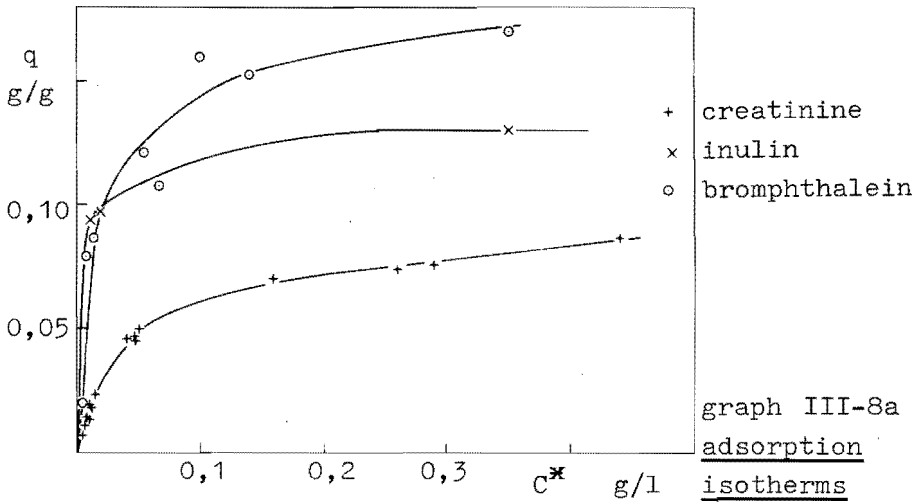
graph III-8b the adsorption isotherm of creatinine
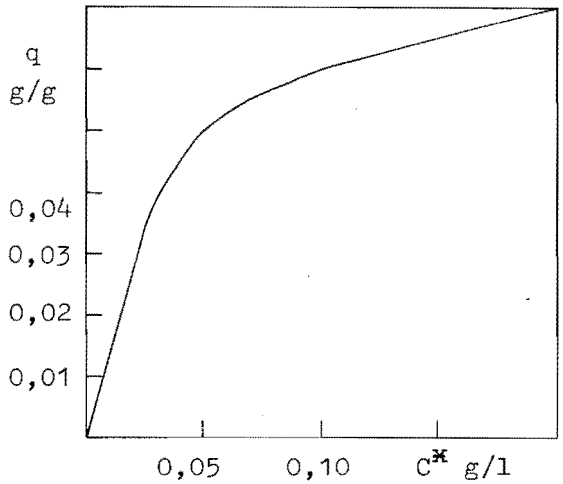
If only adsorption is used for the removal of creatinine from blood, we can now calculate the amount of carbon needed to remove the creatinine produced in the human body in one day (by means of the table I-1). The daily production is about 1 g creatinine and the concentration in blood of uremic patients is about 0,2 g/l. The minimum amount of carbon needed is then 14 g. Since the film adsorber contains 25-30 g of carbon, the production of two days could be removed. This capacity is enough for treatment once every three days if the adsorber is used in combination with a dialyser

III-2-b the diffusion in the liquid

To calculate the diffusion coefficient in a liquid the
formula of Wilke-Chang (H-7) is generally accepted (see
also Bird (H-26)):

$$D_l = 7,4.10^{-12}.TM^{\frac{1}{2}}x^{\frac{1}{2}}/\eta V^{0,6}$$ III-2-1

in which

T is the temperature ^{o}K
M is the molecular weight of the solvent
η is the viscosity   cp
V is the molal volume of the solute   cc/gmol
D is the diffusion coefficient m^2/sec
x is the association number - a correction
  factor for the solvent (2,6 for water)

The molal volume can be calculated by means of Kopp's law,
which states, that the molecular volume is the sum of the
atomic volumes. The atomic volumes are given by Treybal
(H-8) and Lebas (H-22). The molal volumes of creatinine
and uric acid are respectively 117,0 and 145,7. See for
this subject also Perry page 14-20 (H-4).
The diffusion coefficients needed for the description of
the breakthrough curves (the measurement of these curves
is described in paragraph III-3) are for
- creatinine in water of 20°C
  $D=0,845.10^{-9}$ m^2/sec which is in agreement with the va-
  lues of Colton (H-15) and Ikkenberry (H-24) after cor-
  rection for the temperature.
- creatinine in plasma of 37°C $D=0,67.10^{-9}$ m^2/sec
- uric acid in plasma of 37°C $D=0,56.10^{-9}$ m^2/sec
For the diffusion coefficients in blood we will use the
values found by Colton:
- creatinine in blood of 37°C $D=0,53.10^{-9}$ m^2/sec
- uric acid in blood of 37°C $D=0,44.10^{-9}$ m^2/sec

III-2-c the masstransfer coefficient in the liquid

For a laminar flow through a pipe with a temperature fall
at the wall Nusselt (H-10) and Graetz (H-11) have derived,
that the Nusselt number must be constant with a value of
3,65 except for the entrance region. For a flow between
parallel planes this constant Nusselt number is derived by
Hahneman (H-12) and this value is also given by Grigull
(H-13) as 3,75.
Similar calculations are among others performed by Colton
(H-15) and Kooyman (H-23) for masstransfer. Kooyman calcu-
lated a Sh number (kd_1/D_1) of 3,77 for $LD_1/d_1^2\bar{v} > 10^{-1}$ and
a constant concentration boundary condition. In our case
$LD_1/d_1^2\bar{v} = 42$ and the constant Sherwood number may be ap-
plied.

III-2-d the diffusion in the acc film

The measurement of the diffusion coefficient in the acc
film was performed in a so called stirred membrane diffu-
sion cell (SMDC), which is sketched in figure III-1.
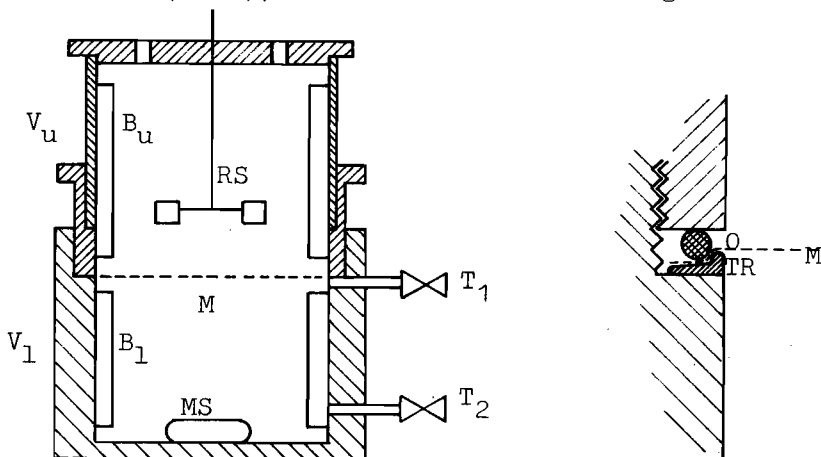
figure III-1 the stirred membrane diffusion cell

The cell consists of two compartments V_u and V_l, which are separated by a membrane M. The membrane is placed in the SMDC as follows:

-Teflon ring TR is put in the wall of V_l. Membrane M is placed upon the teplon ring together with rubber ring O. The wall of V_u is screwed in the wall of V_l. The membrane is streched between the rings TR and O.

V_l is stirred with a magnetic stirrer MS and V_u with a Rushton stirrer RS. For the increase of the stirring effect baffles are placed in both compartments (B_u and B_l). Injections with a dye showed that complete mixing is attained in less than a second. This does not include the boundary layers present at both sides of the membrane surface.

It may be assumed that the overall masstransfer resistance across the membrane is the sum of the mass transfer resistance in the membrane and those of the liquid films sothat

$$1/k_o = d_f/D_m + 1/k_{fl} + 1/k_{fu} \qquad \text{III-2-2}$$

in which

k_o is the overall masstransfer coefficient

d_f is the thickness of the membrane

D_m is the diffusion coefficient in the membrane

k_{fl} and k_{fu} are the masstransfer coefficients in the liquid phases

D_m containes also an distribution coefficient for the distribution of creatinine between the water and the collodion. It is however impossible to measure this coefficient in an acc membrane, because the amount of solute present in the water - collodion system would only be about one percent of the amount adsorbed at the carbon, which is the reason why we took this up in the diffusion coefficient. For the calculation of the masstransfer coefficient in the liquid a number of models is available. The calculation is performed in section III-2-d1. We furthermore controlled these calculated coefficients by means of the measurement

of the overall masstransfer coefficient for a cuprophane
membrane, of which the diffusion coefficient is known from
the litterature. The measurement of the diffusion coeffi-
cient in the acc membrane is described in section III-2-d2.
Furthermore the diffusion coefficient in a pure collodion
membrane is measured as a comparison.

III-2-d1 the boundary_layer_masstransfer coefficient

We used the following models for the calculation of the
masstransfer coefficient in the boundary layers:
a the model of_Kaufman
Kaufman (H-19) found the following equation for the liquid
masstransfer coefficient near a membrane in a stirred cell

$$k_f d_s/D = 0,368(\eta/\rho D)^{0,32}(d_s^2 n\rho/\eta)^{0,68} \qquad \text{III-2-3}$$

in which

k_f is the boundarylayer masstransfer coefficient m/sec
D is the diffusion coefficient in the liquid m^2/sec
d_s is the diameter of the stirrer m
η is the viscosity Nsec/m^2
ρ is the density of the liquid kg/m^3
n is the velocity of rotation rev/sec

The Reynolds number in the upper compartment is 3120 and
in the lower compartment 1700, while d_s is respectively
2,6 and 2,2. The masstransfer coefficients are
$k_{fu}=2,39.10^{-5}$ m/sec and $k_{fl}=1,93.10^{-5}$ m/sec.
For equation III-2-2 we need $1/k_{fu} + 1/k_{fl} = 0,94.10^5$ sec/m.

b the model of_Colton
Colton (H-15,20) came to the following equation:

$$k_f d_c/D = 0,73(\eta/\rho D)^{0,33}(d_c^2 n\rho/\eta)^{0,567} \qquad \text{III-2-4}$$

in which d_c is the diameter of the stirred cell. Calcula-
tions render the following result: $k_{fl}=2,05.10^{-5}$ m/sec and
$k_{fu}=2,3.10^{-5}$ m/sec, while $1/k_{fu} + 1/k_{fl} = 0,92.10^5$ sec/m.

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c the model of Strek

Strek (H-21) has developed a model for the heattransfer to the walls of open stirred tank. When we replace the heat transfer by mass transfer we get the following equation:

$$k_f d_c/D = (\eta/\ell D)^{1/3}(d_s^2\ell/\eta)^{2/3}(d_s/d_c)^{0,13} \; x$$
$$x \; (h/d_c)^{0,12} \qquad\qquad III-2-5$$

in which h is the distance of the stirrer to the tank bottom. Further calculation renders the following result (because the tank should be open the model cannot be applied for the lower compartment): $k_{fu}=2,83.10^{-5}$ m/sec.
The values of the masstransfer coefficients are also shown in table III-4 together with the mean values of the three models.

As mentioned these theoretical values can be controlled by means of measuring the overall masstransfer coefficient for a cuprophane PT150 membrane. This was done as follows. The cuprophane membrane was stretched between the compartments. V_1 was filled with water via tap T_2, while the air was driven out via tap T_1. At the time t=0 V_u was filled with an aqueous creatinine solution. At different times samples were drawn from V_u. In appendix 4 a formula is derived for the calculation of the overall masstransfer coefficient from the measured concentrations in the samples. A correction factor is applied for the sampling.

From graph III-10 it may be concluded that the overall mass transfer coefficient for the cuprophane is $0,261.10^{-5}$m/sec. The diffusion coefficient in water saturated cuprophane is measured by Babb (H-17,18) as $0,164.10^{-9}$ m^2/sec, Colton (H-5) as $0,154.10^{-9}$ m^2/sec and Lande (H-16) as $0,154.10^{-9}$. $1/k_{fu}+1/k_{fl}$ can now be calculated by means of equation III-2-2. Since $d_f=44.10^{-6}$ m, it follows that $1/k_{fu} + 1/k_{fl}$ $=0,91.10^5$ sec/m, which corresponds very well with the value of the mentioned models (see table III-4)

table III-4 <u>the masstransfer coefficients in the liquid</u>

model	$k_{fu} \cdot 10^5$ (m/sec)	$k_{fl} \cdot 10^5$	$(1/k_{fb}+1/k_{fl}) \cdot 10^{-5}$ (sec/m)
Kaufman	2,39	1,93	0,94
Colton	2,30	2,05	0,92
Strek	2,83		
mean value	2,51	1,99	0,89
cuprophane			0,91

III-2-d2 <u>the diffusion coefficient in the acc membrane</u>

It is now possible to calculate the diffusion coefficient
from a measurement of the overall masstransfer coefficient
by means of equation III-2-2.
Because of the adsorption at the carbon the measuring of
the diffusion coefficient in the acc film cannot be car-
ried out in unsteady state and therefore the measuring
method has to be modified. The SMDC was applied in the ex-
perimental set up sketched in figure III-2.
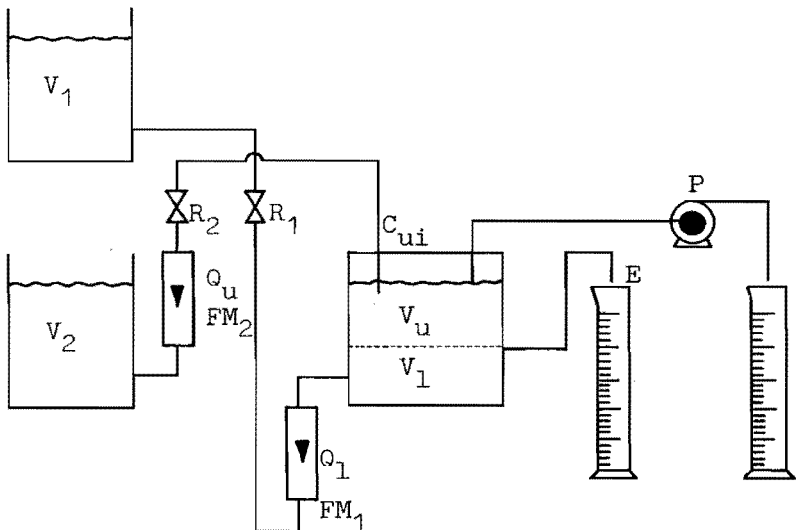
figure III-2   <u>the measurement of the diffusion in the acc</u>
<u>film</u>

An acc membrane was stretched between V_u and V_l. Water was brought in both compartments (V_u=100 ml and V_l=80 ml).
From t=0 an aqueous creatinine solution (C_{li}=0,1 g/l) was led through V_l with a volumetric flowrate Q_l=1 ml/min from container V_1. Q_l was measured by means of rotameter FM_1 and regulated with restiction R_1. For the accurate measurement of Q_l the solution coming out of V_l is received in a calibrated cylinder.
From t=0 pump P pumpes water out of V_u with a volumetric flowrate Q_u=1 ml/min. The water level in V_u remains constant, because it is siphoned over from a container V_2, where the level, which is at the same height as the level in V_u, remains constant because of its large diameter, 0,25 m. The drop of the liquid level is about 1 mm/h. The amount of liquid pumped from V_u was also received in a calibrated cylinder.
No ultrafiltration takes place, since the end of the drain of V_l (E) is at the same height as the water level of V_u.
At different times the concentrations in the output of V_u and V_l (respectively C_{uo} and C_{lo}) are measured.
After a certain time adsorption equilibrium will be reached in the membrane and the concentration in V_u and V_l will remain constant (steady state). In that case:

$$Q_l C_{li} = Q_l C_{lo} + Q_u C_{uo} \qquad\qquad \text{III-2-6}$$

When the steady state is reached anywhere in the membrane it may be assumed, that there is also adsorption equilibrium on the activated carbon. In that case the presence of the carbon particles only causes a barrier for the diffusion through the membrane.
In this case it may be assumed that

$$Q_l(C_{li}-C_{lo}) = Q_u C_{uo} = k_o A(C_{lo}-C_{uo}) \qquad\qquad \text{III-2-7}$$

and the mass transfer coefficients can be calculated.
In graph III-9 the following variables are plotted as a function of time:

$I = \int_0^t Q_l C_{li} dt$ - the amount of creatinine fed to the SMDC

$U_l = \int_0^t Q_l C_{lo} dt$ - the amount carried out through the outlet of V_l

$V_l C_{lo}$ - the amount of creatinine present in V_l

$O = I - U_l - V_l C_{lo}$ - the amount of creatinine transferred through or adsorbed in the membrane

$U_u = \int_0^t Q_u C_{uo} dt$ - the amount of creatinine carried out through the outlet of V_u

$V_u C_{uo}$ - the amount of creatinine present in V_u

$q = O - U_u - V_u C_{uo}$ - the amount of creatinine adsorbed by the membrane during the experiment

These variables are also given in table III-5.
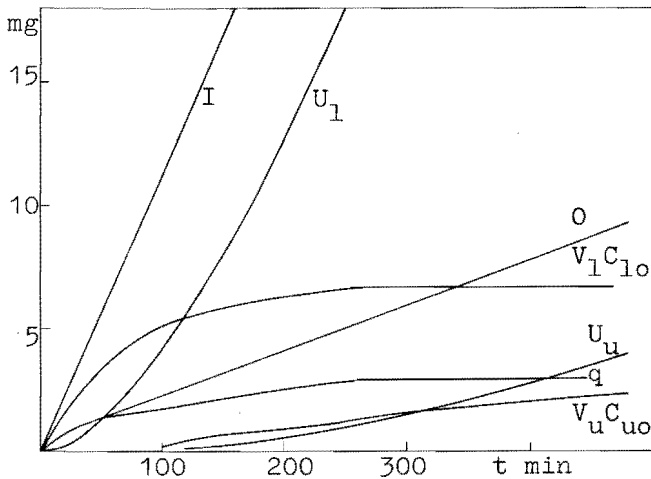
graph III-9 the masstransfer through the acc membrane

Since only after 100 minutes a measurable amount of crea-
tinine comes in V_u, while the steady state is reached af-
ter 300 minutes, it must be concluded, that the adsorption
rate is very fast as compared with the diffusion rate.
From table III-5 may be concluded that $k_o = 0,254.10^{-5}$ m/sec. ·
Since $d_f = 130$ μ the effective diffusion coefficient calcu-
lated with equation III-2-2 seems to be $0,425.10^{-9}$ m^2/sec.

Table III-5 <u>the mass transfer through the acc membrane</u>

the amounts in this table are given in mg; the time in min

t	I	U_l	V_lC_{lo}	0	U_u	V_uC_{uo}	q
20	2,34	0,18	1,48	0,68			0,68
40	4,53	0,89	2,76	0,88			0,88
60	6,32	1,72	3,72	1,38			1,38
80	9,05	2,88	4,52	1,65		0,05	1,65
100	11,3	4,22	5,06	2,00		0,22	1,78
120	13,5	5,67	5,40	2,42	0,11	0,44	1,88
140	15,6	7,11	5,68	2,82	0,19	0,60	2,03
160	18,0	8,81	5,92	3,22	0,30	0,71	2,21
180	20,5	10,7	6,08	3,68	0,42	0,82	2,43
200	23,1	12,7	6,24	4,12	0,56	0,93	2,53
220	25,7	14,8	6,40	4,5	0,71	1,10	2,70
240	28,3	16,9	6,55	4,8	0,88	1,15	2,82
260	30,9	19,0	6,65	5,2	1,07	1,27	2,86
280	33,4	21,1	6,68	5,6	1,27	1,43	2,89
300	35,8	23,2	6,7	5,9	1,50	1,54	2,92
320	38,2	25,2	6,7	6,3	1,72	1,65	2,96
340	40,6	27,2	6,7	6,7	1,97	1,76	2,98
360	42,8	29,1	6,7	7,0	2,22	1,87	2,98
380	45,1	30,9	6,7	7,5	2,49	1,93	3,03
400	47,3	32,8	6,7	7,8	2,77	2,04	3,01
420	49,6	34,7	6,7	8,2	3,07	2,15	2,97
440	51,8	36,5	6,7	8,6	3,38	2,24	2,94
460	54,0	38,4	6,7	8,9	3,70	2,29	2,93
480	56,2	40,2	6,7	9,3	4,03	2,37	2,90

As a comparison we measured the overall masstransfer coefficient in two collodion membranes. The measurement was performed as with the cuprophane membranes.
The first collodion membrane had a mean thickness of 57 μ .
The overall masstransfer coefficient was $0,51.10^{-5}$ m/sec (see graph III-10). The diffusion coefficient is then cal-

graph III-10 the diffusion in membranes
collodion o (V_{ui}=100 cm^3,C_i=0,2 g/l,120μ), • (100, 0,21,57)
cuprophane □ (100, 1, 44), × (100, 0,2, 44), + (75, 0,2,
44), ☆ (90, 0,2, 44)
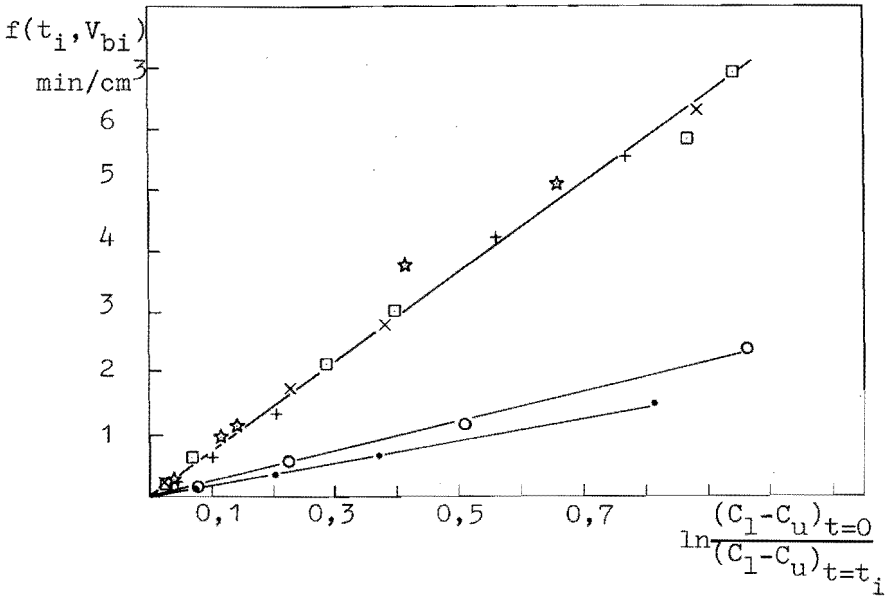
culated with equation III-2-2: 0,54.10^{-9} m^2/sec.
The second membrane had a thickness of 120 μ . The measured
masstransfer coefficient was 0,34.10^{-5} m/sec. The diffu-
sion coefficient is then 0,56.10^{-9} m^2/sec.
Ikkenberry (H-24) found, that the logarithme of the diffu-
sion coefficient of creatinine at 37°C for several membra-
nes plotted against (1/hydration) gives a straight line
(see line a of graph III-11). The change of the temperatu-
re into 25°C renders line b of graph III-11. The values of
the diffusion coefficients, that we measured, are given in
the same graph. They agree very well with line b.

$D_m \cdot 10^9$
m^2/sec

0,5
0,3
0,2
0,1

1   2   1   3

hydration
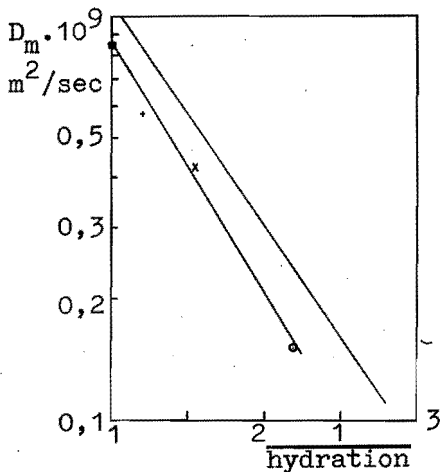
× acc film
+ collodion
⊕ cuprophane
◻ in water following Wilke-
   Chang (H-7)

graph III-11 the diffusion
of creatinine in membranes
following Ikkenberry (H-24)

III-2-e the masstransfer in the carbon particles

A conclusion from the experiment with the acc membrane
described in section III-2-d was, that the adsorptionrate
at the carbon is fast as compared with the masstransport
through the membrane.
We performed the following experiment to measure the ad-
sorption rate at activated carbon from an aqueous solution.
Activated carbon was suspended in half a litre of water.
At time t=0 half a litre of a creatinine solution was ad-
ded to this well stirred suspension. Samples were drawn
from the suspension and filtrated. The sampling and the
filtration took 15 seconds. The creatinine concentration
in the filtrate was measured and is given in graph III-12
as a function of time.
In a first approximation the course of the concentration
in the liquid can be cescribed by the following equation:

$$dC/dt = k_c a_c (C - C^{\divideontimes})$$ III-2-8

in which
C is the concentration in the liquid   g/l
t is the time   min
k_c is the masstransfer coefficient   cm/min
a_c is the specific surface cm^{-1}
$C^{\divideontimes}$ is the concentration in equilibrium with the
   amount adsorbed by the carbon   g/l

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C
g/l
0,2

0,1

1   2   t min
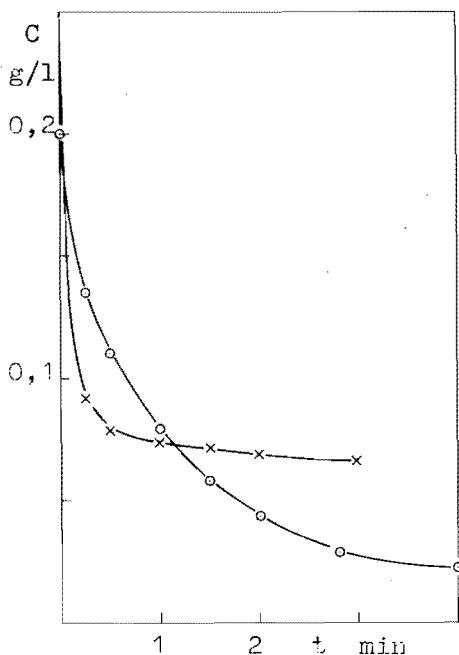
○ C_i=0,2 g/l   10 g_c/l
× C_i=0,3 g/l   5 g_c/l

graph III-12 <u>the masstrans-
fer in the carbon particles</u>

dC/dt is measured from graph III-12 and C^* from graph
III-8b. In table III-6 equation III-2-8 is used to cal-
culate the masstransfer coefficient, which as can be
seen is not constant for the following reasons:

<u>a</u> By means of equation III-2-8 an overall masstransfer co-
efficient is calculated, that will be composed of the
masstransfer coefficient in the liquid surrounding the
carbon particles and the diffusion coefficient in the
particles. When $Fo=tD/d^2>0,05$ the total masstransfer ra-
te will be settled by the internal diffusion. In that
case $Sh=kd/D=6,6$.
The internal diffusion coefficient may be estimated to
be $0,5.10^{-10}$ m^2/sec. The internal diffusion will then
already settle the masstransfer after 1,6 sec (d=40 μ)
and the mean masstransfer coefficient is $0,825.10^{-5}$
m/sec

<u>b</u> The carbon particles will have a distribution in diame-

ter. When the smaller particles are saturated, the larger ones will still adsorb creatinine. Because of the decrease of the liquid concentration the smaller particles will release creatinine and a smaller masstransfer coefficient will be the consequence. To get an impression of this effect we worked out the following examples. Suppose we suspend two fractions with a different particle diameter. The following equations then describe the course of the concentration.

$$-dC/dt = k_1 a_1 (C-C_1^*) + k_2 a_2 (C-C_2^*) \qquad \text{III-2-9}$$

$$\epsilon_1 m dC_1^*/dt = k_1 a_1 (C-C_1^*) \qquad \text{III-2-10}$$

$$\epsilon_2 m dC_2^*/dt = k_2 a_2 (C-C_2^*) \qquad \text{III-2-11}$$

under the following conditions:

$$t=0: \quad C=C_0, \ C_1^*=C_2^*=0$$
$$t=\infty: \quad C^*=C_0/[1+(m-1)(\epsilon_1+\epsilon_2)] \qquad \text{III-2-12}$$

In these equations are

C the concentration in the liquid

m the equilibrium coefficient; $C^*=mC_c$ if C_c is the concentration in the carbon

ϵ the volume fraction of the carbon

k the overall masstransfer coefficient

For C_1^* the following equation results if $\epsilon_1=\epsilon_2$

$$(\epsilon^2 m^2/k_1 a_1 k_2 a_2)d^3 C_1^*/dt^3 + m(1/k_1 a_1 + 1/k_2 a_2)(1+\epsilon m) \times$$
$$\times \ d^2 C_1^*/dt^2 + (1+2\epsilon m)dC_1^*/dt = 0 \qquad \text{III-2-13}$$

The solution of this equation is:

$$C_1^* = C_0/[1+2(m-1)\epsilon] + \{-C_0[1-2w(v+w)]/[1+2(m-1)] +$$
$$+ 2k_1 a_1 C_0 w/\epsilon m\}e^{(v+w)t} + \{2C_0 w(v+w)/[1-2(m-1)] -$$
$$- 2k_1 a_1 C_0 w/\epsilon m\}e^{(v-w)t} \qquad \text{III-2-14}$$

in which

$$v = -(k_2 a_2 + k_1 a_1)(1+\epsilon m)/2\epsilon^2 m \qquad \text{III-2-15}$$

and

$$w = \sqrt{(k_1 a_1 + k_2 a_2)^2 (1+\epsilon m)^2 / 4 \epsilon^4 m^2 - } $$
$$ - \overline{(1+2\ m)k_1 a_1 k_2 a_2 /\ ^2 m^2} \qquad\qquad \text{III-2-16}$$

A similar equation is found for $C_2^{\textstyle *}$.
After substitution of $C_1^{\textstyle *}$ and $C_2^{\textstyle *}$ in equation III-2-9 a so-
lution for C could be found.
Application of two fractions, however, is not enough to
find the course of the masstransfer coefficient as given
in table III-6. At least five fractions with different
diameters are needed to explain this course. A solution
like III-2-14 should be rather difficult for five frac-
tions. We therefore simulated experiment a of table III-6
in another way. We started with the following assumptions:
- the carbon (10 g in 1 litre) is distributed as follows
  0,5 g with a mean diameter of 10 μ
  2   g with a mean diameter of 25 μ
  5   g with a mean diameter of 40 μ
  2   g with a mean diameter of 55 μ
  0,5 g with a mean diameter of 70 μ
- the masstransfer is limited by the internal diffusion so
  that Sh=6,6
- the internal diffusion coefficient is $0,5.10^{-10}$ m^2/sec
- the initial liquid concentration is 0,2 g/l
- every fraction has a different value of $k_o a$ as listed in
  table III-7.
It is now possible to calculate $(dC/dt)_{t=0}$. We suppose,
that this concentration gradient is maintained for twen-
ty seconds and thus C after twenty seconds can be calcu-
lated. The total amount of creatinine, that is adsorbed is
now calculated. The part, which each fraction adsorbs is
the same as the part, which each fraction contributes to
the adsorption rate (dC/dt). By means of graph III-8b the
concentration in equilibrium with each fraction is known.
And again dC/dt can be calculated. And so on every twenty
seconds. We can also calculate a mean equilibrium concen-

tration every twenty seconds and thus by means of equation
III-2-8 a mean value of k_oa.
All these values are listed in table III-7 and we see,
that the course of the concentration with time, but also
the course of k_oa with time corresponds very well with the
measured values.
Our conclusion is, that the variations of the overall mass
transfer coefficient is mainly caused by the variation in
diameter of the carbon particles.

Table III-6 <u>the masstransfer in the carbon particles</u>

t	C	dC/dt	q	C^{*}	$C-C^{*}$	k_oa	$k_o.10^5$
min	g/l	g/lmin	g/g$_c$	g/l	g/l	min^{-1}	m/sec
<u>a</u> 0	0,2	0,4	0	0	0,2	2	2,2
0,25	0,135	0,136	0,0065	0,003	0,132	1	1,1
0,5	0,111	0,079	0,0090	0,004	0,106	0,74	0,81
1	0,079	0,057	0,0121	0,006	0,073	0,78	0,86
1,5	0,058	0,037	0,0142	0,007	0,051	0,72	0,79
2	0,043	0,024	0,0157	0,008	0,035	0,69	0,76
3	0,028	0,008	0,0172	0,008	0,020	0,40	0,44
4	0,022	0,004	0,0178	0,009	0,013	0,35	0,38
<u>b</u> 0	0,3	1	0	0	0,3	3,33	7,4
0,25	0,092	0,124	0,041	0,033	0,059	2,10	4,7
0,5	0,079	0,021	0,044	0,038	0,041	0,51	1,1
1	0,074	0,009	0,045	0,040	0,034	0,26	0,58
1,5	0,071	0,005	0,046	0,043	0,028	0,18	0,40
2	0,069	0,004	0,046	0,044	0,025	0,17	0,38
3	0,066	0,003	0,047	0,045	0,021	0,12	0,27

<u>a</u>: C_i=0,2 g/l ; 10 g of carbon/l ; a=1500 m^2/m^3
<u>b</u>: C_i=0,3 g/l ; 5 g of carbon/l ; a= 750 m^2/m^3

g_c is the volume amount of carbon

table III-7 <u>the calculated masstransfer in the carbon</u>

t	C	q_1	q_2	q_3	q_4	q_5	$c_1^\ast$
0	0,200	0	0	0	0	0	0
0,2	0,145	0,0470	0,0075	0,0030	0,0015	0,0010	0,05
0,4	0,110	0,0600	0,0183	0,0051	0,0026	0,0016	0,10
0,6	0,093	0,0620	0,0173	0,0065	0,0033	0,0020	0,103
0,8	0,080	0,0600	0,0203	0,0077	0,0040	0,0022	0,10
1,0	0,070	0,0566	0,0222	0,0084	0,0045	0,0024	0,08
1,2	0,061	0,0544	0,0243	0,0093	0,0050	0,0026	0,07
1,4	0,054	0,0524	0,0260	0,0101	0,0054	0,0028	0,062
1,6	0,047	0,0508	0,0267	0,0108	0,0058	0,0031	0,050
1,8	0,042	0,0504	0,0286	0,0113	0,0061	0,0033	0,050
2,0	0,037	0,0482	0,0297	0,0119	0,0064	0,0035	0,047
2,2	0,034	0,0460	0,0304	0,0123	0,0066	0,0037	0,043
2,4	0,031	0,0444	0,0311	0,0127	0,0068	0,0039	0,040
2,6	0,029	0,0426	0,0315	0,0130	0,0070	0,0041	0,035
2,8	0,027	0,0414	0,0319	0,0133	0,0071	0,0042	0,032
3,0	0,026	0,0408	0,0321	0,0135	0,0072	0,0043	0,032

t	$c_2^\ast$	$c_3^\ast$	$c_4^\ast$	$c_5^\ast$	dC/dt	$\overline{c}^\ast$	$\overline{k_o a}$
0	0	0	0	0	0,278	0	1,39
0,2	0,0040	0,0020	0,0010	0	0,176	0,0031	1,24
0,4	0,0077	0,0028	0,0015	0,0010	0,095	0,0050	0,90
0,6	0,0900	0,0036	0,0018	0,0010	0,067	0,0060	0,77
0,8	0,0113	0,0043	0,0020	0,0010	0,051	0,0067	0,69
1,0	0,0123	0,0047	0,0025	0,0013	0,047	0,0072	0,74
1,2	0,0135	0,0052	0,0028	0,0014	0,039	0,0077	0,74
1,4	0,0145	0,0056	0,0030	0,0016	0,034	0,0081	0,74
1,6	0,0153	0,0060	0,0032	0,0017	0,030	0,0085	0,77
1,8	0,0159	0,0063	0,0034	0,0018	0,022	0,0088	0,67
2,0	0,0165	0,0066	0,0035	0,0020	0,017	0,0090	0,61
2,2	0,0169	0,0068	0,0037	0,0021	0,014	0,0091	0,56
2,4	0,0173	0,0071	0,0038	0,0022	0,011	0,0094	0,52
2,6	0,0175	0,0072	0,0039	0,0022	0,011	0,0096	0,57
2,8	0,0180	0,0074	0,0039	0,0023	0,010	0,0096	0,56
3,0	0,0200	0,0076	0,0040	0,0024	0,007	0,0097	0,46

fraction	d (μ)	weight (g)	K (m/sec)	a (m^2/m^3)	$k_o a (min^{-1})$
1	10	0,5	$3,3 \cdot 10^{-5}$	300	0,595
2	25	2	1,32	480	0,380
3	40	5	0,82	750	0,375
4	55	2	0,60	218	0,078
5	70	0,5	0,47	43	0,012

The 10 g of carbon was suspended in 1 l of creatinine so-
lution. $\rho = 1$ g/cm^3

III-3 Breakthrough curves

We have now relations, with which it is possible to calcu-
late each mechanism, that is important for the description
of the functioning of the film adsorber. For the integra-
tion of these mechanisms two models are available.
The first model (see section III-3-a) gives by means of
curve fitting of a measured breakthrough curve and theore-
tical curves a value for the overall masstransfer coeffi-
cient. In section III-3-d this value for four breakthrough
curves, of which the measurement is described in section
III-3-c is compared with an overall masstransfer coeffici-
ent calculated from the parameters described in paragraph
III-2.
The second model (see section III-3-b) gives the possibi-
lity to calculate the mean residence time and the variance
for a breakthrough curve. In section III-3-d the measured
values are again compared with the values calculated by
means of this model.

III-3-a the model of Vermeulen

Vermeulen (H-2,3) has developed a model for an adsorption
column, in which a component is transfered from the liquid
phase into a solid granular material.
From t=0 the column is flown by a liquid with a solute (in-
put concentration C_i). The concentration of the component
is calculated as a function of time and place in the co-
lumn. The following assumptions are made:
- there is no axial dispersion in the column
- the concentration of the component is uniform in each
  particle (in the present case uniform in the solid phase
  in a cross section of the adsorber); all masstransfer is
  thus described with a constant masstransfer coefficient
- the concentration of the component in the liquid is uni-
  form in a cross section of the column in each channel.

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A material balance over a part dz of the column renders
the following equations:

$$\varepsilon_e \partial C / \partial t = -v_o \partial C / \partial z - k_o a_f (C - C^{\textbf{x}})$$ III-3-1

for the liquid phase and

$$\rho_b \partial q / \partial t = k_o a_f (C - C^{\textbf{x}})$$ III-3-2

for the solid phase, in which

ε_e is the external porosity (volume of the liquid phase
per unit volume of the column)

C is the concentration in the liquid phase

v_o is the superficial velocity

k_o is the overall masstransfer coefficient

a_f is the specific surface of the acc film $(2 \varepsilon_e / d_1)$

ρ_b is the weight of the carbon per unit volume of the co-
lumn

q is the concentration of the solute in the solid phase
(given per unit weight of the carbon)

$C^{\textbf{x}}$ is the concentration of the solute in the liquid phase
in equilibrium with the concentration in the solid
phase

For the solution of these equations the following dimen-
sionless variables are applied:

X the dimensionless liquid concentration C/C_i

Y the dimensionless solid phase concentration $q/q_i^{\textbf{x}}$, in
which $q_i^{\textbf{x}}$ is the concentration, when the column is in
equilibrium with C_i

N_z the number of masstransfer units: $k_o a_f z / v_o$

Θ the time modulus or solution parameter:

$$\Theta = k_o a_f C_i (t - \varepsilon_e z / v_o) / \rho_b q_i^{\textbf{x}}$$

If $C = f(\Theta, N)$ and $\Theta = f(t, z)$, $N = f(z)$ then

$$\frac{\partial C}{\partial t} = \frac{\partial C}{\partial \Theta} \cdot \frac{\partial \Theta}{\partial t} + \frac{\partial C}{\partial N} \cdot \frac{\partial N}{\partial t} \text{ and } \frac{\partial C}{\partial z} = \frac{\partial C}{\partial \Theta} \cdot \frac{\partial \Theta}{\partial z} + \frac{\partial C}{\partial N} \cdot \frac{\partial N}{\partial z}$$ III-3-3

By means of equation III-3-3 the equations III-3-1 and
III-3-2 are transformed into

$$-(\partial X / \partial N)_\Theta = X - Y \text{ and } (\partial Y / \partial \Theta)_N = X - Y$$ III-3-4

The following initial and boundary conditions should be applied:

1)   on t=0   q=0   for 0<z<L

  or Θ=0   Y=0   all N_z

2)   on z=0   C=C_i for t>0

  or N_z=0   X=1 Θ>0

The solution of these equations is (see also Mickley (H-27)) X=J(N,Θ) and Y=J(Θ,N)   III-3-5

with

$$J(\nu,t)=1-\int_0^\nu e^{-t-\xi} I_0 2\sqrt{t\xi}d\xi \qquad \text{III-3-6}$$

in which I_0 is the Bessel function of order zero and the first kind.

A similar equation can be derived for non linear equilibrium relations, in which case the equilibrium parameter r is introduced as defined by

$$Y^*=X/(r+(1-r)X) \qquad \text{III-3-7}$$

in which $Y^*=q^*/q_i^*$

Using the adsorption isotherm (graph III-8b) it is found, that r=0,2.

For a number of values of r Vermeulen has calculated X as a function of N and Θ. In most cases, however, one is interested in the overall masstransfer coefficient for a column of known length, in which case $N_L=k_o a_f L/v_o$ is used instead of N_z

Since both variables N and Θ contain the factor $k_o a_f$ a new variable is introduced: the throughput parameter Z

$$Z=\Theta/N_L=C_i v_o(t-\epsilon_e L/v_o)/L\ell_b q_i^* \qquad \text{III-3-8}$$

The parameter Z is unity when the column is passed by a volume, that is stoichiometrically equal to the adsorption capacity. This is easier to see, if equation III-3-8 is rewritten:

$$Z=C_i(V-\epsilon_e v)/\ell_b q_i^* v \qquad \text{III-3-9}$$

in which v is the volume of the column and V the volume of

the liquid, which passed the column.

Vermeulen has plotted X at the output of a column as a function of Z with N and r as parameters. By means of curve fitting N can be found for a measured breakthrough curve (see also Perry (H-4)).

In section III-3-d this method is used to find $k_o a_f$ for the measured breakthrough curves of section III-3-c. The values found this way are compared with the masstransfer and the diffusion coefficients described in paragraph III-2. In graph III-15 X is plotted against Z for some values of N and for r=0,2.

III-3-b the model of Kucera

Kucera (H-5) has developed a model to predict the course of the concentration of a compound as a function of time and place in a section of a chromatographic column filled with porous grains of uniform size and the shape of among others infinite plates with a thickness d=2R.

Kucera, in contrast with Vermeulen, considered four mass transfer mechanisms (see figure III-3):
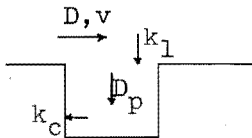
figure III-3 the mass transfer mechanisms in the pores following Kucera

a diffusion and convection in the free volume
b masstransfer from the free volume into the plates
c diffusion in the pores of the plates
d sorption at the wall of the pores.

We can translate these masstransfer mechanisms in (see figure III-4):

ad a the diffusion and convection in the liquid film

$$\delta C_1/\delta t + (v_o/\varepsilon_e)(\delta C_1/\delta z) - D_p \delta^2 C_1/\delta z^2 = -\Phi_1 \quad \text{III-3-10}$$

in which

C_1 is the concentration in the liquid film

t is the time

v_o is the superficial velocity

ϵ_e is the external porosity of the acc film (volume of the liquid film per total volume of the column)

Φ_1 is the masstransfer rate into the acc film

D_p is the diffusion coefficient
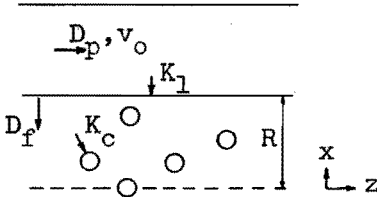
figure III-4 <u>the four mass-transfer mechanisms in the film adsorber</u>

<u>ad b the masstransfer from the liquid into the acc film</u>

$$\Phi_1 = K_1(m_1 C_1 - C_{f(x=R)}) \qquad\qquad \text{III-3-11}$$

in which

K_1 is a massexchange coefficient: in our case $K_1 = k_1 a_f / \epsilon_e$
  in which
  k_1 is the masstransfer coefficient as described in section III-2-c
  a_f is the specific surface of the acc film ($2\epsilon_e/d_1$)
m_1 is a equilibrium coefficient: we choose $m_1 = 1$ (see for explanation section III-2-d)
C_f is the concentration in the film (given per unit volume of the film)

The massflux into the acc film is $j_f = -D_f(\delta C_f/\delta x)_{x=R}$, in which D_f is the diffusion coefficient in the acc film (see section III-2-d) and thus

$$\epsilon_e \Phi_1 = -j_f a_f = [(1-\epsilon_e)D_f/R](\delta C_f/\delta x)_{x=R} \qquad \text{III-3-12}$$

in which R is half of the thickness of the acc film

<u>ad c diffusion in the acc film</u>

$$\delta C_f/\delta t - D_f \delta^2 C_f/\delta x^2 = -\Phi_c = \delta q/\delta t \qquad \text{III-3-13}$$

in which Φ_c is the sorption rate in the carbon particles.

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ad d the masstransfer_from the water in_the_acc_film into
   the carbon_particles

$$\Phi_c = K_c(m_c'C_f - q) \qquad\qquad\qquad III\text{-}3\text{-}14$$

in which

K_c is a massexchange coefficient: $k_c a_c$ (see section
   III-2-e)

q is the concentration of the compound in the carbon gi-
   ven per unit volume of the water in the acc film and q
   is thus smaller then when it is given per unit volume
   of the carbon

m_c' is an equilibrium coefficient defined by

$$m_c' = m_c g_c / \epsilon_i Lbd_f \qquad\qquad\qquad III\text{-}3\text{-}15$$

   in which

   m_c is the equilibrium coefficient as given by graph
   III-8b

   g_c is the volume amount of carbon in the acc film

   ϵ_i is the internal porosity of the acc film

Next to equation III-3-12 another boundary condition is
needed for the calculation of the course of the concentra-
tion $\quad (\partial C_f / \partial x)_{x=0} = 0 \qquad\qquad\qquad III\text{-}3\text{-}16$

Furthermore the following initial conditions are needed:
$C_1(z,t) = C_f(x,z,t) = q(x,z,t) = 0 \quad$ for $t<0$ and $z = \pm \infty$

$$\left.\begin{array}{l} C_1(z,t) = C_{1i}(z) \\ C_f(x,z,t) = C_{fi}(z) \\ q(x,z,t) = q_i(z) \end{array}\right\} \quad \text{for } t=0 \quad -\infty < z < +\infty \quad 0 < x < R \quad III\text{-}3\text{-}17$$

where $C_{1i}(z)$, $C_{fi}(z)$ and $q_i(z)$ describe the initial dis-
tribution of the introduced compound.

Kucera applies now Laplace transformation defined by:

$$C^+ = \int_0^\infty Ce^{-pt}dt \qquad\qquad\qquad III\text{-}3\text{-}18$$

In general it is impossible to carry out the inverse trans-
formation and to find an analytical expression for C_1. It

is, however, possible to calculate μ_k' (the k-th moment) of the function $C_1(t)$ defined by

$$\mu_k' = u_k/u_o \quad \text{where } u_k = \int_0^\infty t^k C(t)dt \qquad \text{III-3-19}$$

Let μ_k be the k-th central moment defined by

$$\mu_k = \frac{1}{u_0}\int_0^\infty (t-\mu_1')^k C(t) \qquad \text{III-3-20}$$

Furthermore the following property of the Laplace transformation is known (see also v.d.Laan (H-28)):

$$(-1)^k \lim_{p=0}\frac{d^k C^+(p)}{dp^k} = \int_0^\infty t^k C(t)dt \qquad \text{III-3-21}$$

In this way Kucera calculates the first five central moments. To compare the experimental results of the break-through experiments we used only the first and the second moment:

$$\mu_1 = [L\epsilon_e/v_o + 2D_p\epsilon_e^2/v_o^2][1 + em_1(1+m_c')] \qquad \text{III-3-22}$$

$$\mu_2 = [2D_pL\epsilon_e^3/v_o^3 + 8D_p^2\epsilon_e^4/v_o^4][1 + em_1(1+m_c')] +$$

$$+ [2L\epsilon_e/v_o + 4D_p\epsilon_e^2/v_0^2] \times em_1 \times \qquad \text{III-3-23}$$

$$\times [R^2(1+m_c')^2/3D_f + e(1+m_c')^2/K_1 + m_c'/K_c]$$

in which $e = \epsilon_i(1-\epsilon_e)\epsilon_e$

By means of the following assumptions the equations III-3-22 and III-3-23 will be simplified:
- The terms with D_p are to be neglected. For example the order of magnitude of $L\epsilon_e/v_o$ is one minute and that of $2D_p(\epsilon_e/v_o)^2$ is 10^{-4} minutes
- $m_c'/K_c \ll R^2(1+m_c')^2/3D_f$. m_c'/K_c has an order of magnitude of 20 and $R^2(1+m_c')^2/3D_f$ of 10^3 (see section III-2-e)
- $m_c' \gg 1$ since m'_c is about 100

The following formulas for the first and second moment result:

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$$\mu_1' = \epsilon_i(1-\epsilon_e)Lm_c'/v_o \qquad\qquad \text{III-3-24}$$

$$\mu_2 = 2L\epsilon_i(1-\epsilon_e)m_c'(R^2/3D_f + e/K_1)/v_o \qquad \text{III-3-25}$$

In section III-3-d calculations with these equations are
compared with the experimental values of section III-3-c.
For the experimental values the equations III-3-19 and
III-3-20 were used.

III-3-c the measurement of the breakthrough curves

For the measurement of the breakthrough curves the set up
of figure III-5 was used.
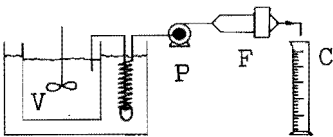
figure III-5 the measurement
of the breakthrough curves

From vessel V a solution of the model solute was led by
pump P through a coil O (to adjust the temperature) and
through the film adsorber F into a calibrated cylinder C.
At different times samples were drawn from the output of
the film adsorber and the volume of the output was measu-
red. Three kinds of experiments were performed:
a An aqueous creatinine solution with a volumetric flow
  rate of 30 ml/min was led through the film adsorber at
  25°C (input concentration 0,1 g/l).
b An aqueous creatinine solution (0,1 g/l) was led through
  a film adsorber with a volumetric flowrate of 100 ml/min
  at 25°C. At the moment, that the film adsorber was satu-
  rated the input concentration was suddenly increased up
  to 0,2 g/l. This last step was done to compare the amounts
  adsorbed at the saturation points with the adsorption
  isotherm. This last step is, however, not included in
  the theoretical analysis.

<u>c</u> Bovine blood was led through the film adsorber with a
volumetric flowrate of 60 ml/min at 37°C. The input cre-
atinine concentration was 0,2 g/l and the input urate
concentration was 0,1 g/l.

For these experiments three different adsorbers were used
of which the data are given in table III-8-a.

The output concentrations are shown in graph III-13 and
the quantities, that were adsorbed in graph III-14.

× III-3-ca
o III-3-cb
□ III-3-cc
  creatinine
—III-3-cc
  uric acid
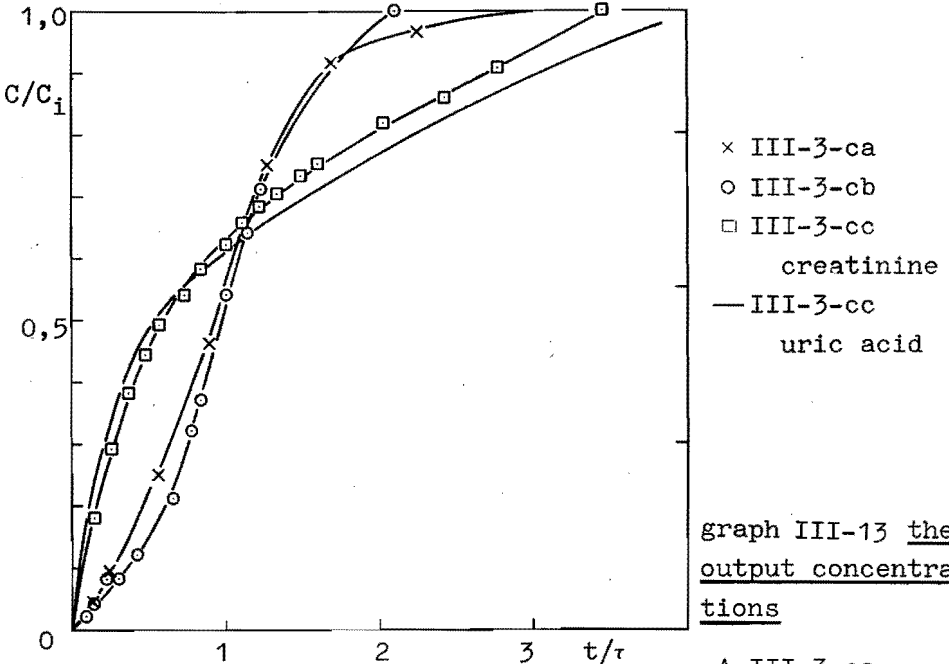
graph III-13 <u>the
output concentra
tions</u>
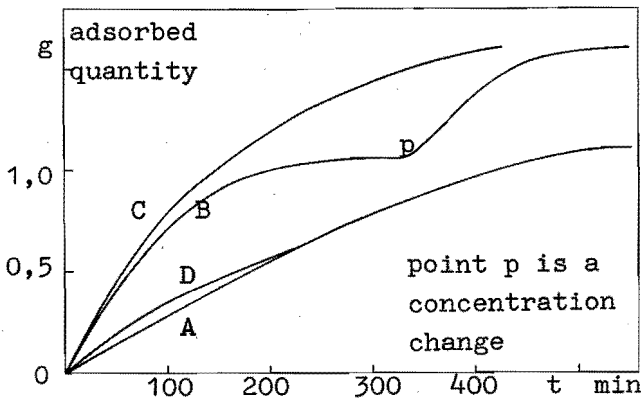
A III-3-ca
B III-3-cb
C III-3-cc
  creatinine
D III-3-cc
  uric acid

graph III-14 <u>the
adsorbed quan-
tities</u>

point p is a
concentration
change

III-3-d <u>conclusions from the breakthrough curves</u>

The parameters needed for the interpretation of the break-
through curves are given in table III-8-a.
<u>the model of Vermeulen</u>
By means of these parameters the curve fitting procedure,
as described in section III-3-a, is applied (see graph
III-15).
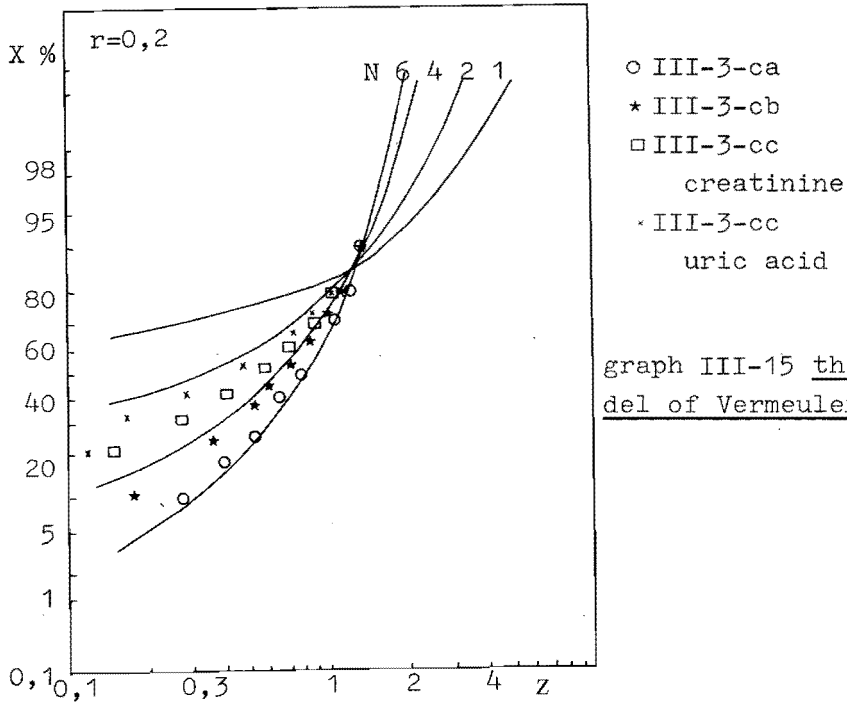
graph III-15 <u>the mo-
del of Vermeulen</u>

In this way we find the number of masstransfer units and a
value for the overall masstransfer coefficient as shown in
table III-8-b.
These values can be compared with the masstransfer coeffi-
cient as described in paragraph III-2 by means of the fol-
lowing equation:

$$1/K = 1/k_1 a_f + d_f/2D_f a_f \qquad\qquad III-3-26$$

In this equation the term for the masstransfer in the car-

bon particles is neglected. The use of $\frac{1}{2}d_f$ is of course an arbitrary decision, since the penetration deepness will change during the course of the experiment.

The values for K calculated by means of equation III-3-26 are shown in table III-8-b. It is seen, that the calculated K is only a indication for the practical value and also the determined value for the number of masstransfer units is only an indication for the real value.

This is to be expected because of the assumptions made during the development of the model. Especially the assumption of a constant masstransfer coefficient does influence the result.

the model of Kucera

Since we have no adsorption isotherm measured for uric acid, we used the measured value of the first moment to calculate the equilibrium constant m_c' by means of equation III-3-24. For creatinine this value of m_c' can be compared with the value calculated by means of equation III-3-15 (also by means of the adsorption isotherm). This last value of m_c' was used to calculate the value of μ_2 by means of equation III-3-25.

μ_2 (calculated) is again compared with the measured value of μ_2 from the breakthrough curves. All these values are shown in table III-8-c. As seen from this table the two values for m_c' are in good agreement, whereas for the two values of μ_2 only the order of magnitude is well.

Comparison of the two models

The model of Vermeulen is a good means to get an impression of the number of masstransfer units. Since the model is simple as compared with the Kucera model, it is easy to handle in practical circumstances.

The model of Kucera gives a good value for the mean residence time, if as in the case of creatinine the equilibrium constant is known. The values of μ_2 give only an order of magnitude.

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Since it was only possible to get an rough impression of
the number of masstransfer units and the residence time by
means of these models, we did not try to optimize the film
adsorber.

table III-8 the breakthrough curves

  a the adsorbers

parameters	III-3-ca	III-3-cb	III-3-cc creatinine	III-3-cc uricacid
$L.10^2$ m	9,6	9,6	9,6	9,6
b m	10	8,3	9	9
$d_f.10^6$ m	155	155	150	150
$d_1.10^6$ m	34	74	62	62
ϵ_e	0,18	0,324	0,293	0,293
ϵ_i	0,65	0,65	0,65	0,65
$v_0.10^4$ m/sec	2,5	8,2	4,8	4,8
C_i g/l	0,1	0,1	0,2	0,1
g_c cm^3	25,9	21,6	22,9	22,9
q_i^* g/gram carbon	0,06	0,06	0,07	0,045
$a_f.10^{-2}$ m^{-1}	102	85	93	93
$D_f.10^9$ m^2/sec	0,425	0,425	0,337	0,228
$k_1.10^5$ m/sec	9,3	4,3	3,2	2,6

  b the model of Vermeulen

$Z./t.10^5 sec^{-1}$	3,11	11,9	11,4	8,9
N_L	6	4	3	2,5
$k_o a_f.10^2$ sec^{-1}	1,5	4,2	1,5	1,25
$K.10^2$ sec^{-1} (calculated by III-3-26)	5,0	4,2	3,1	2,9

  c the model of Kucera

$\mu_1'.10^{-3}$ sec	25,2	7,4	8,7	10,5
m_c' (from μ_1')	125	142	93	112
m_c' (from graph III-8b)	141	148	90	
$\mu_2.10^{-7}$ sec^2 (by means of theory)	3,7	1,23	1,15	2,4
$\mu_2.10^{-7} sec^2$ (measured)	11,5	1,55	5,57	11,3

C H A P T E R IV

PRECLINICAL ANALYSIS OF THE FILM ADSORBER

IV-1 Adsorption of some metabolites and ions from blood

In chapter III experiments have been described with model
solutes. Now the adsorption of some metabolites from bovi-
ne blood will be described. For this purpose we used the
experimental set up as sketched in figure IV-1.
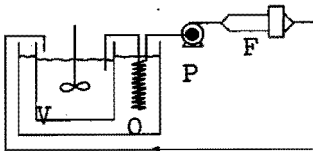
figure IV-1 the experimental set up
for the recirculation of a liquid
through the film adsorber

From vessel V (containing 5 litres of bovine blood) blood
was recirculated by means of roller pump P through a coil
O (to adjust the temperature at $39^{o}C$) and film adsorber F.
The levels of creatinine, urate and urea were elevated
respectively up to 0,16 g/l, 0,08 g/l and 1 g/l.
The volumetric flowrate was set at 60 ml/min. Each 15 mi-
nutes a sample of 10 ml was drawn from the vessel.
For urate, creatinine, glucose and total protein the con-
centration is shown in graph IV-1 as a function of time.
The adsorption of K^{+}, HCO_3^{-}, Ca^{++}, phosphate and urea was
not detectable.
The initial clearance of uric acid, creatinine and glucose
was respectively 31 ml/min, 50 ml/min and 7 ml/min, while
in 200 minutes 0,3 g, 0,6 g and 0,95 g was respectively
adsorbed of these solutes. Equilibrium was reached for to-
tal protein within two hours (when 11 g was adsorbed).

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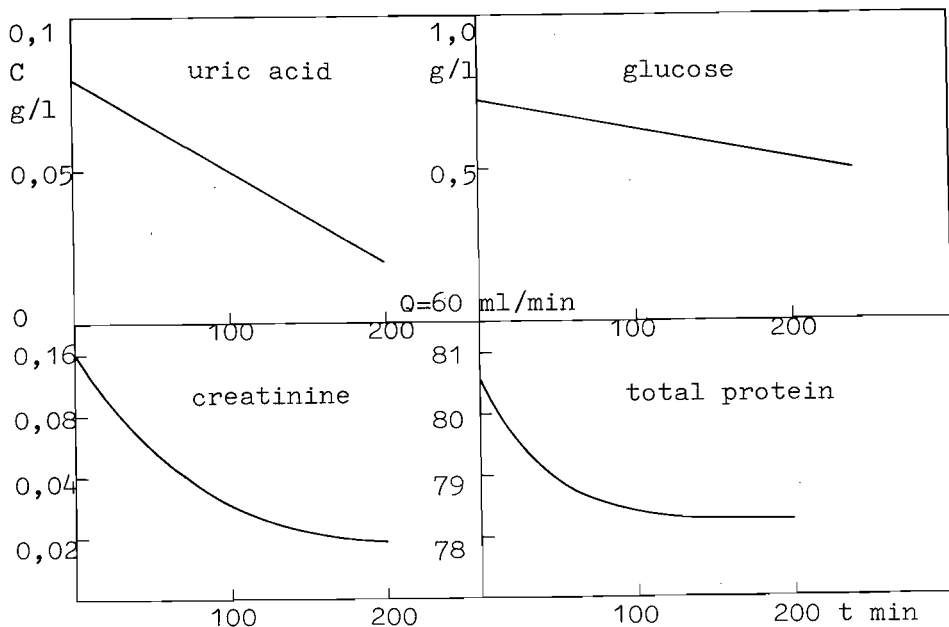
graph IV-1 <u>adsorption of some solutes from bovine blood</u>

IV-2 <u>Adsorption of albumin</u>

In the experiment described in paragraph IV-1, it was
found, that 11 g of total protein was adsorbed by the film
adsorber. It is to be expected, that about the same amount
will be adsorbed, when the film adsorber is used for the
removal of poisons from human blood.
We therefore performed some experiments with albumin, to
find out wether the adsorption takes place at the collo-
dion or at the carbon particles.
To find out, which possibility is true, the following
three cartridges were used in the experimental set up as
sketched in figure IV-1:
<u>1</u> a cartridge (described in section II-2-c) filled with
   100 acc sheets
<u>2</u> a cartridge filled with 100 collodion sheets
<u>3</u> the adsorber with the film roll
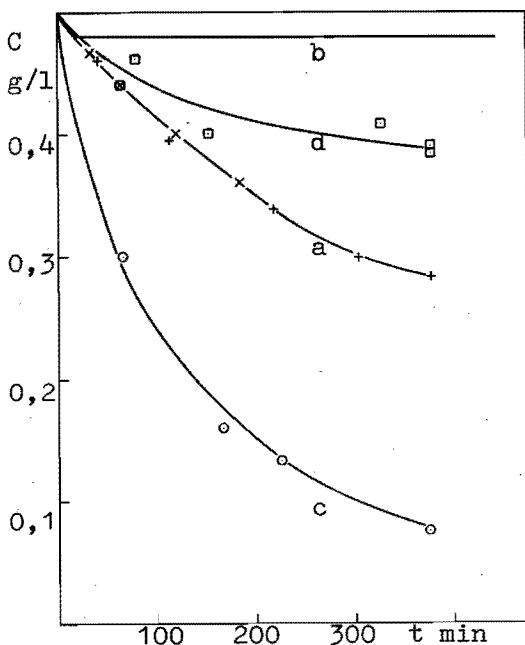
a + adsorption by collodi-
    on and acc sheets
a × adsorption by the film
    adsorber
b   circulation without
    adsorber
c ○ adsorption of inulin
d ☐ adsorption after sa-
    turation with dextran

graph IV-2 the adsorp-
tion of albumin

Through each of these appararatus 3 litres of an albumin
solution was recirculated at 25°C (initial concentration
in each experiment 0,5 g/l). The albumen concentration in
the vessel was measured after different time intervals
(see graph IV-2).
We used the sheet adsorber, because it is easier to make
collodion sheets, than to make a collodion film roll. One
must, however, be careful to draw conclusions from the ex-
periments 1 and 2, because
- the sheet adsorber gives no reproduceable results (as
  descibed in section III-2-c)
- the free carbon at the edges of the sheets might influ-
  ence the results.
In spite of these reasons the experimental data of the
three experiments lead to the same curve (curve a in graph
IV-2).
The decrease in concentration of the albumen is not the
result of the albumin biodegradation as follows from the

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curve b in graph IV-2, which shows the albumin concentra-
tion as a function of time during recirculation under the
same conditions but without the adsorber in the circuit.
The conclusion is, that the adsorption takes place at the
collodion and that no albumen is adsorbed at the activated
carbon. It is, however, well known that also in the hemo-
dialyser adsorption takes place at the semipermeable mem-
brane.
The adsorption of inulin by means of the sheet adsorber
under the same conditions is given in graph IV-2 for com-
parison (curve c), from which can be concluded, that in
this case the adsorption takes place at the carbon parti-
cles as well.
To diminish the adsorption at the acc film we carried out
the following experiment:
Half a litre of a dextran solution was recirculated during
a couple of hours through a film adsorber. Thereafter the
dextran solution was exchanged for 3 litres of an albumen
solution (initial concentration 0,5 g/l) and the concen-
tration in the vessel was measured as a function of time.
As is seen from curve d of graph IV-2 the adsorption capa-
city was decreased by 50% under these conditions. We did
not try to optimize this result by applying different
kinds of dextran and different kinds of concentrations.
Neither did we study the effect of dextran, when blood is
flown through the adsorber.

IV-3 Hemolysis caused by the film adsorber

In order to measure hemolysis during recirculation of bo-
vine blood through the film adsorber the same experimental
set up was used as described in the last paragraph.
Hemolysis can be detected by measuring the free hemoglobin
level.
We found that if bovine blood was stored at $4^{\circ}C$ some hemo-
lysis occured. The daily increase of the free hemoglobin

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level under these conditions was about 0,02 mmol/l. Besi-
des the red blood cells became weaker, so that we measured
an enormous hemolysis, when we used bovine blood, that was
stored a couple of days.
We decided therefore to use fresh heparinized blood. Two
experiments (each with half a litre of blood) were perfor-
med: one with a volumetric flowrate of 30 ml/min and an
other with a volumetric flowrate of 60 ml/min and both at
37°C. Once every 10 minutes samples were drawn from the
vessel. The course of the free hemoglobin level is shown
in graph IV-3. This level varies in the human body between
0,003 and 0,025 mmol/l, while levels up to 0,05 are accep-
table. These values are found after sampling, which might
cause hemolysis as well.

× 30 ml/min

∘ 60 ml/min
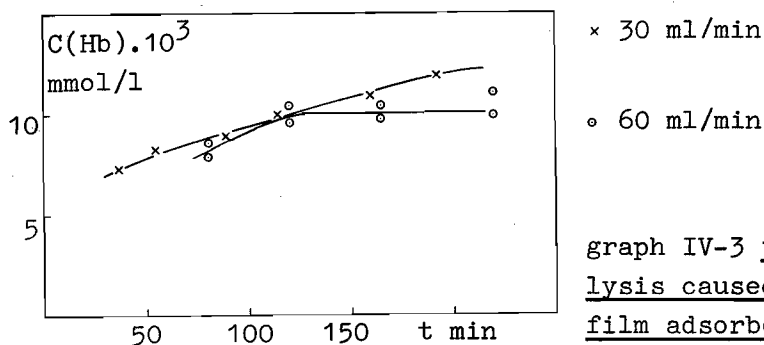
graph IV-3 <u>the hemo-
lysis caused by the
film adsorber</u>

It might be possible that not all free hemoglobin is de-
tected during the experiments, because the film adsorber
might adsorb hemoglobin.
To that end solutions with various hemoglobin levels were
prepared by means of dilution of hemolysed blood with
plasma. The solutions were shaken with acc sheets. Before
and after the shaking the hemoglobin levels were measured
and no significant difference could be detected, which in-
dicates that adsorption of hemoglobin at the collodion is
negligible.
Since we found no increase of the free hemoglobin level

during circulation of bovine blood through the circuit
without the film adsorber, the slight hemolysis, that was
detected during circulation of bovine blood in the above
described experiments, is probably caused by the film ad-
sorber. This amount of hemolysis is, however, of no im-
portance.

IV-4 Release of carbon particles and glass beads by the film adsorber

The release of glass beads has never been noticed during
the experiments. This is also hardly to be expected, be-
cause they cannot pass between the windings of the roll,
since their mean size is four to five times that of the
mean distance between the windings.
It might be possible for a released glass bead to escape
from the adsorber (the design, that we used - see figure
II-1), although the settling rate of a glass bead is one
cm/sec and the rate of the blood is 0,1 cm/sec during the
leaving of the roll. The rate of the blood is, however,
8,5 cm/sec in the outlet of the adsorber.
A better design of the outlet is sketched in figure IV-2.
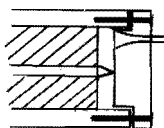
figure IV-2 a design of the
outlet, through which the glass
beads can not pass

However also with this design small particles with a set-
tling rate smaller than 0,1 cm/sec could be transported by
the blood flow and not be noticed because of their small
size.
In order to detect a possible release of carbon particles
the experimental set up of figure IV-1 was used again. A
filter, through which the particles could not pass, was
placed after the film adsorber. Half a litre of a saline

solution was recirculated through the film adsorber with a flowrate of 100 ml/min. After eight hours the film adsorber was replaced by an other one and the same solution was recirculated again.

The first adsorber was rinsed with twenty litres of water before use, while the second was immediately used after assembling.

Through a third adsorber an aqueous solution of glycerol with a viscosity of 20 cp was recirculated with a volumetric flowrate of 100 ml/min.

No particles were found on the filter after the adsorbers. Our conclusion is therefore, that the film adsorber does not release carbon particles direct after assembling. Neither does the rinsing of the film adsorber cause a release of carbon particles. Also when higher viscosities (as in blood) are used, we arrive at the same conclusion.
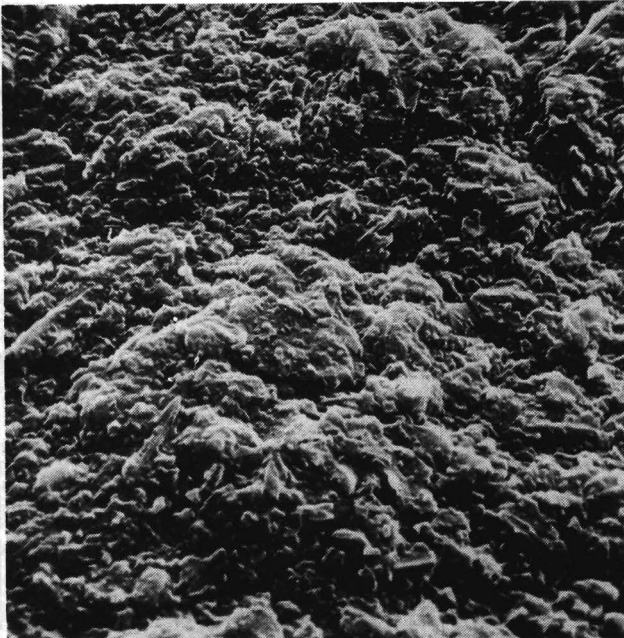
picture IV-1 the acc film surface (390x)
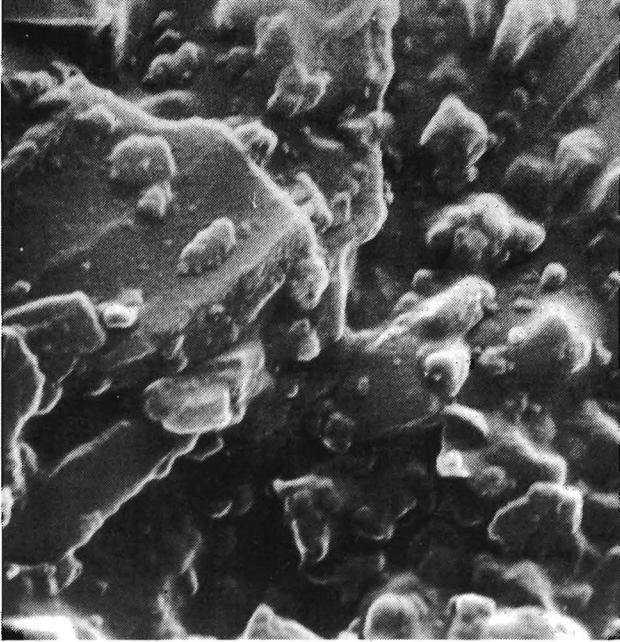
picture IV-2 <u>the</u>
<u>acc film surface</u>
<u>3900x</u>
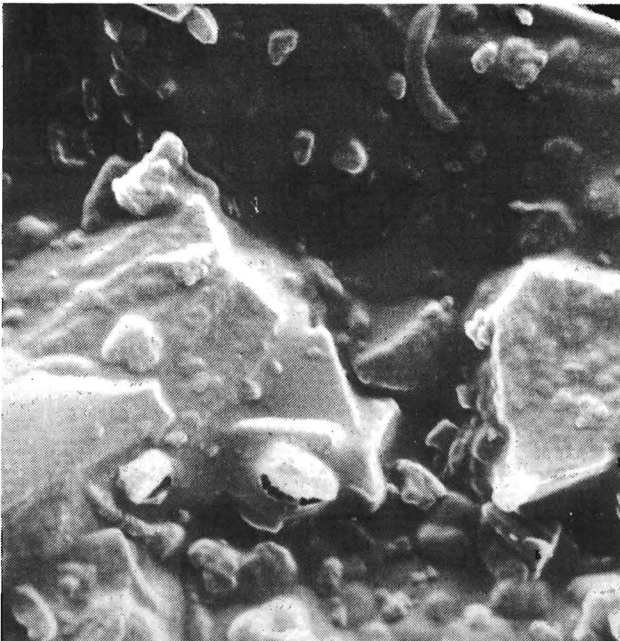
picture IV-3 <u>the</u>
<u>acc film surface</u>
<u>4300x</u>

The pictures IV-1, IV-2 and IV-3 give evidence, that it is realy unlikely, that carbon particles are released from the acc film. These pictures were made by means of a scanning electron microscope after drying of the acc film.and they give an enlargement of the acc film surface (IV-1: 390x, IV-2: 3900x, IV-3: 4300x).
Picture IV-3 was taken after that the electron beam was burned into the acc film.
The pictures show that the outside of the acc film consists of an collodion layer covering the carbon particles, as was expected from the way of production. This collodion layer has a thickness of about 0,1 μ (in the dry film) and it has no edges.

IV-5 The competition effect

It was suggested, that there might be a competition for adsorption between different metabolic products, so that one metabolite might supersede an other. This is very likely at high concentrations, but hardly to be expected at the relatively low concentrations of the metabolites in the blood.
Already van Leer (C-4) did not find a significant competition effect. Only when he added a large amount of creatinine to a suspension of carbon in a glucose solution he found a desorption of glucose. He did not found, however, that glucose caused desorption of creatinine.
To detect a possible competition effect in the film adsorber we used again the experimental set up sketched in figure IV-1. The vessel was filled with half a litre of a saline creatinine solution (1 g/l) and the circulation throughput was 100 ml/min. The equilibrium liquid concentration was 0,014 g/l.

Next 1 g of glucose was added to the solution in the vessel. After 6 hours the creatinine concentration was still 0,014 g/l. Also the addition of 6 g urea to the solution in the vessel did not change the creatinine concentration. In section IV-1 was already shown, that there is no influence on the adsorption of creatinine by other metabolites. Our conclusion is that the competition effect does not have an important influence.

IV-6 The adsorption of barbiturates by the film adsorber

In general exogenous poisons will be good adsorbed at activated carbon because of their relatively high molecular weight. Among others Chang (E-7, E-14), Yatzidis (C-9) and Widdop (J-8) mention the good adsorption qualities of an activated carbon containing system for a lot of pharmaca. Some experiments were performed to prove the applicability of the film adsorber for the removal of these pharmaca from blood. We used phenobarbital and secobarbital, because these barbiturates have a different adsorption capacity at the plasma proteins as is seen in appendix 7. In this appendix some other data about barbiturates are given as well.

We used the sodium form of the mentioned barbiturates. All concentrations are related to that form.

In section IV-6-a the measurement of the adsorption isotherms of the barbiturates at free carbon is described and in section IV-6-b some experiments with the film adsorber.

IV-6-a the adsorption isotherms of barbiturates at free carbon

The adsorption isotherms were determined as described in section III-2-a and the measurements were performed in water, plasma and blood. The adsorption isotherms are plot-

graph IV-4 the adsorption isotherm of phenobarbital
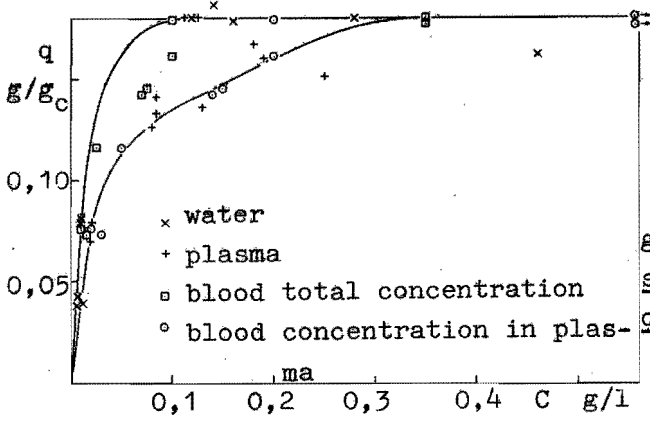
q g/g$_c$

× water
+ plasma
□ blood total concentration
○ blood concentration in plasma
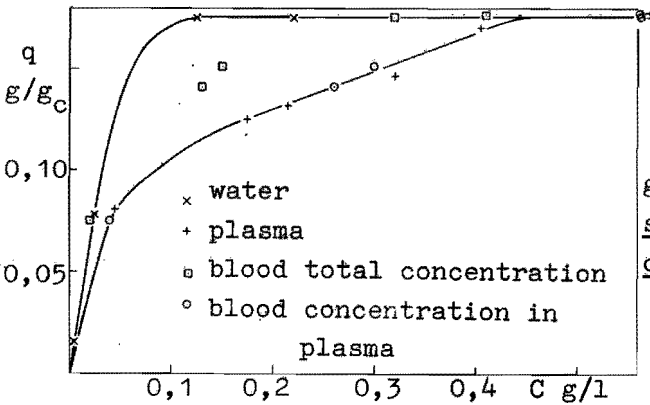
graph IV-5 the adsorption isotherm of secobarbital

q g/g$_c$

× water
+ plasma
□ blood total concentration
○ blood concentration in plasma

ted for water and plasma in graph IV-4 and graph IV-5. The measurement of the concentrations involves the measurement of the amount of barbiturate in a unit volume of dispersion (see appendix 2). This holds for the measurement in blood too. As the barbiturates will hardly enter the blood cells the concentration in the plasma is twice as high as the measured concentration if the hematocrit amounts to 50. It is the concentration in the plasma, which is the real equilibrium concentration.

This is in agreement with the graphs IV-4 and IV-5, as the measurements with blood fit with the measurements with plasma after correction for the hematocrit.

Barbiturates are also adsorbed by plasma proteins. In appendix 7 the percentage of adsorption is given as found by Goldbaum (J-7). The adsorption at activated carbon will be

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influenced by this phenomenom. At equilibrium the amount, that is adsorbed, will be in equilibrium with the concentration of free barbiturate. This holds if the amount of protein, that is adsorbed at the carbon is negligible.
By means of the concentration measurement total barbiturate concentrations are measured, thus inclusive the barbiturates adsorbed at the proteins. We can therefore calculate the percentage of this adsorption from the graphs IV-4 and IV-5.
If one reads the value of the equilibrium concentration in water at a specific amount of barbiturate adsorbed at the carbon, this value must be the same as the concentration of free barbiturate in plasma. In that case the rest of the total liquid concentration is the concentration of the barbiturate caused by adsorption to the proteins. When we carry out this procedure in the mentioned graphs, we see, that the percentage of the barbiturate adsorbed at the proteins is not constant and mostly higher than the percentages found by Goldbaum (see appendix 7).
We have no explanation for this phenomenom. A possible explanation might be that the result of the concentration measurement depends on the medium in which it is carried out. We checked this, but found that the concentration measurement in plasma and blood agree very well with that of water as can be seen from graph IV-6. In this graph the measured extinction (see appendix 2) is plotted against adjusted concentrations.
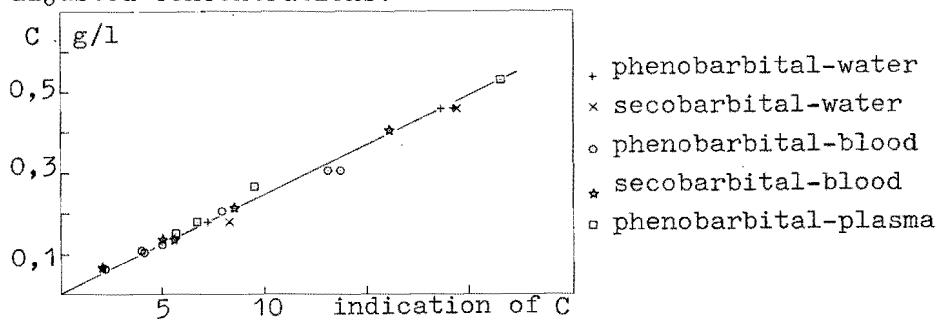
graph IV-6 the quantitative analysis of the barbiturates

+ phenobarbital-water
× secobarbital-water
o phenobarbital-blood
* secobarbital-blood
▫ phenobarbital-plasma

IV-6-b e̲x̲p̲e̲r̲i̲m̲e̲n̲t̲s̲ w̲i̲t̲h̲_t̲h̲e̲_f̲i̲l̲m̲ a̲d̲s̲o̲r̲b̲e̲r̲

For these experiments the same set up was used as in the
preceding paragraphs. The vessel was filled with 5 litres
of a barbiturate solution and the volumetric flowrate was
100 ml/min. The experiment was performed with secobarbital
and phenobarbital both in a buffered saline solution with
a pH of 7 and in blood.
The course of the concentrations in the vessel is shown in
graph IV-7. In table IV-1 the clearance (as calculated
from this graph) and the total amount adsorbed are given
as a function of time.

C_i (g/l)

+ water 0,2
phenobarbital
× blood 0,125

o water 0,1
secobarbital
□ blood 0,1

graph IV-7 t̲h̲e̲ a̲d̲-
s̲o̲r̲p̲t̲i̲o̲n̲ o̲f̲ b̲a̲r̲b̲i̲t̲u̲-
r̲a̲t̲e̲s̲ b̲y̲ t̲h̲e̲ f̲i̲l̲m̲
a̲d̲s̲o̲r̲b̲e̲r̲
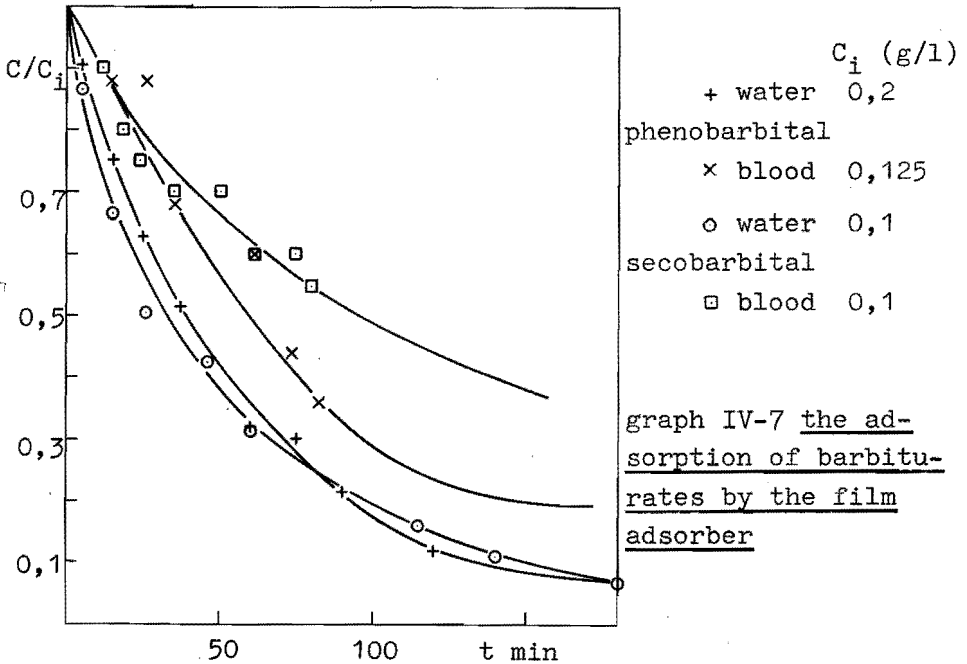
For secobarbital and phenobarbital in water the initial
clearances are 99 and 97,5 ml/min and in blood 51 and 66,5
ml/min respectively. The clearance from blood is less than
that from water, which is the consequence of the adsorp-
tion at the proteins.
Lassen (J-2) found a mean clearance with forced diuresis

Table IV-1

The adsorption of barbiturates by the film adsorber

the adsorption from an aqueous solution

	phenobarbital					secobarbital			
t	C_c	C_f	Cl	q	t	C_c	C_f	Cl	q
0	0,200			0	0	0,1000			0
5	0,181			0,095	5	0,0867	0,0200	97,5	0,066
15	0,150	0,0133	99	0,250	16	0,0665	0,0240	86,5	0,166
25	0,126	0,0166	98,5	0,370	26	0,0504	0,0069	86	0,248
37	0,103	0,1711	98,5	0,485	46	0,0423	0,0106	80	0,228
60	0,073	0,0180	75	0,635	60	0,0312	0,0117	68,5	0,344
75	0,060	0,0155	79	0,700	115	0,0161	0,0045	72	0,419
90	0,043	0,0104	76	0,785	140	0,0111	0,0034	96,5	0,444
120	0,024	0,0060	75	0,880	181	0,0070	0,0034	51,5	0,465
205	0,009	0,0047	50	0,955	220	0,0050	0,0024	52	0,475

the adsorption from bovine blood

	phenobarbital					secobarbital			
t	C_c	C_f	Cl	q	t	C_c	C_f	Cl	q
0	0,100			0	0	0,100	0,034	66	0
14	0,087	0,0425	51,2	0,066	12	0,090	0,038	58	0,05
25	0,082	0,0432	55,4	0,090	18	0,080	0,047	43,7	0,10
35	0,065	0,0284	56,3	0,175	24	0,075	0,047	40,1	0,125
60	0,055	0,0244	61	0,225	35	0,070	0,047	36,8	0,15
75	0,044	0,022	57	0,28	50	0,070	0,046	31,1	0,15
82	0,034	0,018	61,5	0,33	61	0,060	0,044	27	0,2
100	0,032	0,016	56,5	0,34	75	0,060	0,046	23	0,2
150	0,027	0,013	41	0,36	80	0,055	0,043	22	0,225

t is the time (min); C_c is the concentration in the container (g/l); C_f is the concentration in the output of the film adsorber calculated from C_c; Cl is the clearance (ml/min); q is the adsorbed amount.
The volumetric flowrate through the adsorber was 100 ml/min and the temperature was 37°C.

of 8 ml/min and 18 ml/min of phenobarbital and secobarbital respectively. Trautman (J-1) gives for the clearance with a dialyser (membrane surface 1,3 m^2 and volumetric flow rate 200 ml/min) a value of 25 ml/min.

As the clearances found in this study are much higher, the film adsorber seems to be an improvement for the removal of barbiturates.

The clearances may be further elevated by the use of a larger exchanging surface, which can be done without objections because of the small priming volume of the film adsorber.

As the film adsorber does not influence the pH-, the water or the ionbalance of the body fluids, a minimal medical care is needed during the detoxification.

Activated carbon will adsorb organic solutes with a molecular weight above 100 (see section II-1-a). The film adsorber will therefore also remove other poisons. Especially for patients with acute hepatic failure the adsorber might have prospects (see also Gazzard (J-9,10)).

IV-7 The simultaneous use of the film adsorber and a dialyser

In the treatment of uremic patients with a hemodialyser the poor extraction of the metabolites of medium molecular weight (200-5000) is more and more considered as the limiting factor for the dialysis and in fact determines the duration of the dialysis treatment.

Probably the simultaneous use of the film adsorber and the hemodialyser, which is very well possible because of the small priming volume and the large exchanging surface of the film adsorber, gives new prospects. Because the film adsorber eliminates these socalled middle molecules faster than the dialyser as will be shown in this paragraph, the time needed for the dialysis treatment can be reduced. The duration of the treatment will then be fixed by the time

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needed to remove urea and therefore will depend on the
sensitivity of the patient for the desequilibrium syndrome.
Section IV-7-a describes the use of the film adsorber and
the dialyser in series connection. The course of the con-
centration of urea, creatinine, uric acid and bromsulfo-
phthaleine was measured during recirculation of a solution
of these compounds.
Section IV-7-b describes the use of the film adsorber and
the dialyser in parallel connection. The course of the
concentration of urea, creatinine and bromsulfophthaleine
was measured.
Conclusions from these experiments are drawn in section
IV-7-c.

IV-7-a series connection of the film adsorber and the
        dialyser

The set up sketched in figure IV-3 was used. Vessel V is
filled with 5 litres of an aqueous solution of urea, crea-
tinine, uric acid and bromsulfothaleine (BSP) . The ini-
tial concentrations were: urea 1 g/l, creatinine 0,2 g/l,
uric acid 0,1 g/l and BSP 0,1 g/l.
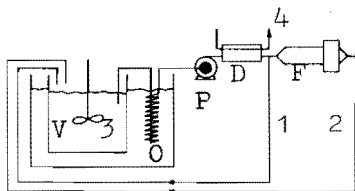
figure IV-3 the series con-
nection of the film adsor-
ber and a dialyser

By means of pump P the solution was led from the vessel
through a coil O (to adjust the temperature at 37°C) and
the dialyser D with a volumetric flowrate of 208 ml/min.
After the dialyser the flow was split up: 100 ml/min was
led through the film adsorber F back into the reservoir;
the remaining part was returned directly into the reser-
voir. The dialysate (temperature 37°C) was led through the
dialyser with a volumetric flowrate of 504 ml/min.

A single pass hemodialyser of the coil type with closed
dialysate side and a membrane area of 0,8 m^2 was used.
Samples were drawn at the points 1, 2, 3 and 4 (see figure
IV-3) and the concentrations in these samples were measu-
red and they are shown in graph IV-8 for urea, IV-9 for
creatinine, IV-10 for uric acid and IV-11 for BSP. The
course of the urea concentration in the vessel is calcula-
ted from the concentrations after the dialyser and the
film adsorber.
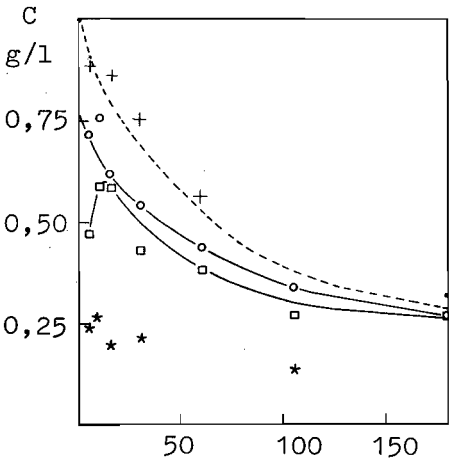
+ in the vessel
o after the dialyser
a after the adsorber
* in the dialysate
------calculated from the con-
       centrations after the dia-
       lyser and the adsorber
graph IV-8 <u>the removal of urea
            - series connection</u>
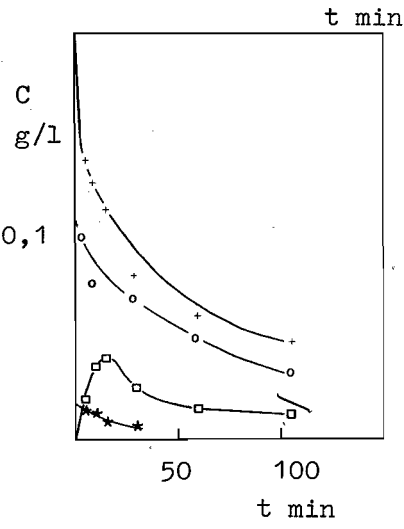
+ in the vessel
o after the dialyser
a after the adsorber
* in the dialysate

graph IV-9 <u>the removal of cre-
            atinine - series
            connection</u>
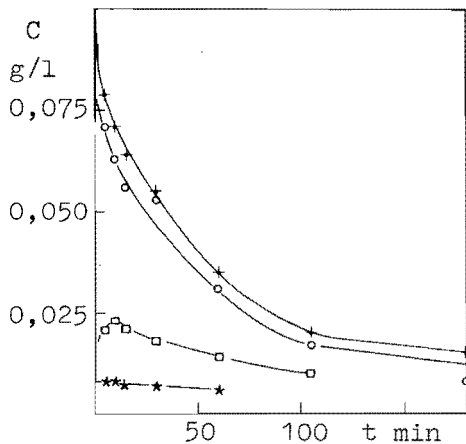
+ in the vessel
∘ after the dialyser
▫ after the adsorber
⋆ in the dialysate

graph IV-10 <u>the removal of</u>
<u>uric acid - series</u>
<u>connection</u>

+ in the vessel
∘ after the dialyser
▫ after the adsorber
⋆ in the dialysate

graph IV-11 <u>the removal of</u>
<u>BSP - series con-</u>
<u>nection</u>

IV-7-b <u>parallel connection of the film adsorber and a</u>
<u>dialyser</u>

The experimental set up sketched in figure IV-4 was used.
Vessel V contains 5 litres of an aqueous solution of urea
(2,0 g/l), creatinine (0,2 g/l) and BSP (0,1 g/l). By
means of pump P the solution was led through coil O to ad-

figure IV-4 <u>the parallel</u>
<u>connection of the film ad-</u>
<u>sorber and a dialyser</u>
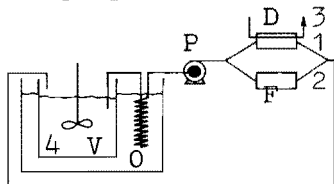
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just the temperature at 39°C. The stream was then split up: one part flows through dialyser D (215 ml/min) and the other part flows through adsorber F (110 ml/min). After passage through the dialyser and the film adsorber the streams are led back into the vessel. The volumetric flow rate of the dialysate (37°C) was 540 ml/min. Samples were drawn at the points 1, 2, 3 and 4 (see figure IV-4). The measured concentrations are shown in graph IV-12 (urea), graph IV-13 (creatinine) and graph IV-14 (BSP).
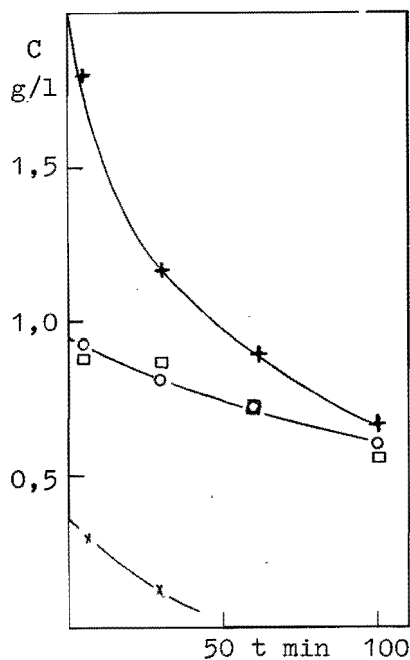
+   in the vessel
o   after the dialyser
□   after the dialyser
×   in the dialysate

graph IV-12 the removal of urea - parallel connection

IV-7-c conclusions from the experiments with the simulta- neous use of the film adsorber and a dialyser

1 The amounts of the solutes, which are removed from the solutions are given in table IV-2. After 100 minutes al- ready 2,85 g of urea, 0,77 g of creatinine, 0,4 g of uric acid and 0,27 g of BSP was removed from the solution in case of the series connection. In the case of the parallel connection 6,5 g of urea, 0,9 g of creatinine and 0,38 g
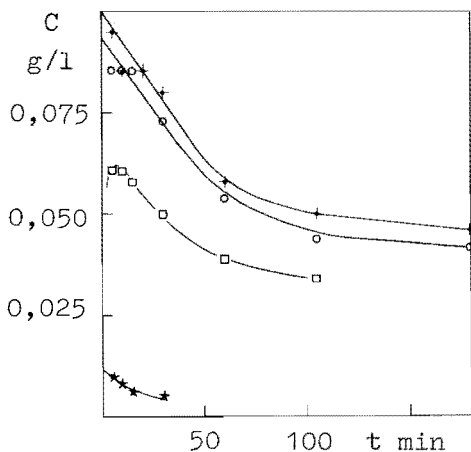
+ in the vessel
∘ after the dialy-
  ser
□ after the adsor-
  ber
× in the dialysate
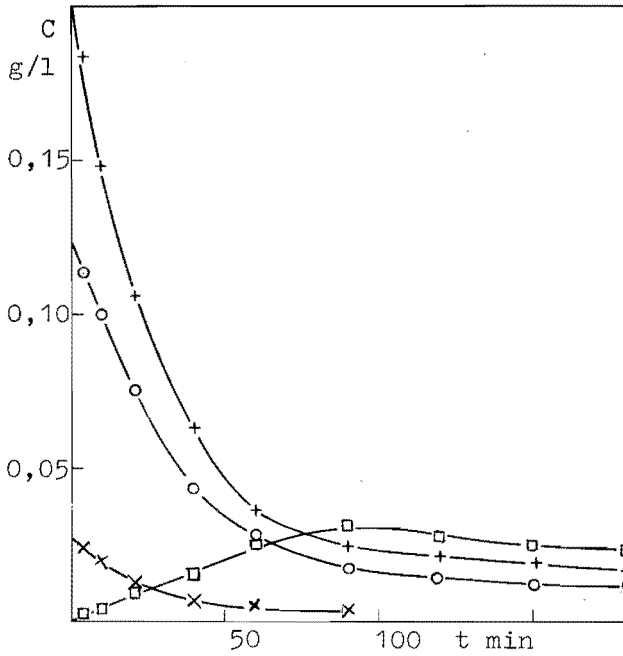
graph IV-13 the re-
moval of creatini-
ne - parallel con-
nection

+ in the vessel
□ after the adsorber
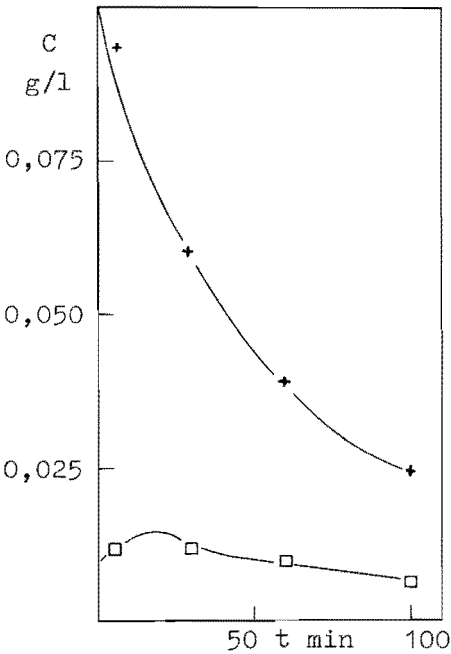
graph IV-14 the removal of
BSP - parallel connection

of BSP is removed after 100 minutes.

Urea is removed in a larger amount in the case of the pa-
rallel connection, because the initial concentration was
two times higher than in the experiment with the series
connection.

There was no significant difference between the in and
output urea concentration in the case of the parallel con-
nection and our conclusion is, that the adsorption of urea
does not have an important contribution to the removal of
urea.

Creatinine is removed in a larger amount in the case of
the parallel connection because of the higher input con-
centration of the adsorber. The difference between the two
experiments is, however, not important in view of the lar-
ge amount of creatinine, that is adsorbed. This holds es-
pecially, since the removal of urea will fix the time
needed for the dialysis treatment.

In the case of the parallel connection the film adsorber
released again creatinine after 75 minutes. The total
clearance, however, still remains positive, since the dia-
lyser still removes creatinine. In vivo experiments will
not show this phenomenom, since the cells of the body will
continuously supply creatinine.

BSP is also removed in a larger amount in the case of the
parallel connection. We have no explanation for this phe-
nomenom.

There is no significant difference between the input and
the output BSP concentration of the dialyser in the case
of the parallel connection and our conclusion is, that the
dialyser has no significant contribution to the removal of
middle molecules from blood.

2 The clearance for the different solutes in the two expe-
riments are shown in table IV-3.

Three different clearances can be defined: one for the di-
alyser (Cl_d), one for the film adsorber (Cl_f) and a total
clearance (Cl_t).

In the case of parallel connection $Cl_t = Cl_f + Cl_d$.
In the case of series connection, however, the following
equation has to be applied:

$$Cl_t = Q_d(C_i - (C_{do} + C_{fo})/2)/C_i \qquad \qquad \text{IV-1}$$

in which

Q_d is the volumetric flowrate through the dialyser
C_i is the input concentration of the dialyser
C_{do} is the output concentration of the dialyser
C_{fo} is the output concentration of the film adsorber.
The film adsorber has a great influence on the total clea-
rance of the middle molecules, but also on the total clea-
rance of the solutes with a molecular weight between 100
and 200.
The film adsorber is therefore a useful addition to the
dialyser, especially since the film adsorber does not have
an important effect on the clearance of urea and therefore
does not increase the risk for the desequilibrium syndrome.

table IV-2 <u>the quantities removed in the case of the si-
multaneous use of dialyser and film adsorber</u>

series connection

t	q_d			q_f		
	creatinine	uric acid	BSP	creatinine	uric acid	BSP
5	0,061	0,007	0,0052	0,050	0,022	0,017
10	0,106	0,016	0,0099	0,080	0,040	0,031
30	0,204	0,047	0,0243	0,155	0,095	0,079
60	0,277	0,079	0,0445	0,272	0,143	0,137
105	0,393	0,117	0,0863	0,394	0,179	0,195

parallel connection

t	q_d		q_f	
	urea	creatinine	creatinine	BSP
10	1,74	0,120	0,175	0,062
30	3,84	0,255	0,380	0,185
60	5,64	0,348	0,482	0,282
105	6,82	0,41	0,475	0,361

table IV-2 continued

total removal (q_t)

	series connection				parallel connection	
t	creatinine	uric acid	BSP		creatinine	BSP
10	0,186	0,056	0,041		0,295	0,062
30	0,359	0,083	0,103		0,635	0,1855
60	0,549	0,212	0,182		0,830	0,282
105	0,787	0,290	0,282		0,885	0,361

the time is given in minutes and q is given in grams.

table IV-3 <u>the clearances in the case of the simultaneous
use of the film adsorber and a dialyser</u>

series connection

t	uric acid			creatinine			BSP		
	Cl_d	Cl_f	Cl_t	Cl_d	Cl_f	Cl_t	Cl_d	Cl_f	Cl_t
5	24	59	61	61	79	119	8,7	34	40
10	26	64	70	57	61	104	10,1	30	43
15	31	62	82	53	53	94	9,5	31	40
30	31	62	84	52	63	100	10,8	30	43
60	28	55	75	51	70	106	11	28	43
105	31	41	68	71	61	116	10	23	50

parallel connection

t	creatinine			BSP	urea
5	Cl_d	Cl_f	Cl_t		
5	83	109	192	85	103
10	69	107	175	79	90
20	61	104	165	75	77
40	65	86	151	74	74
60	67	39	106	76	50
90	69	-22	47	65	32
120	71	-26	45	66	

the clearances are given
in ml/min

C H A P T E R   V

CONCLUSIONS

1 the preparation of the acc film
We have developed an apparatus to prepare the acc film.
This apparatus operates fully automatically. The produced
films have a constant thickness and breadth.

2 the flow distribution
When flown by water the pressuredrop over the adsorber can
be described by the formula for the pressure drop over a
slit for a Newtonian fluid.
When flown by blood the pressuredrop over the adsorber can
be described by the formula for the pressuredrop over a
slit for a Cassonian fluid with the assumption of a margi-
nal plasma layer.
The film adsorber has no dead corners or short circuits of
importance.

3 the masstransfer mechanisms in the film adsorber
A reasonable approximation of the number of masstransfer
units can be made by the model of Vermeulen.
The mean residence time of a solute can be calculated by
means of the model of Kucera for breakthrough curves.

4 the adsorption capacity of the film adsorber
All metabolites are good adsorbed by the film adsorber.
The only exception is urea.
If the daily production of creatinine in men is 1 g and
the concentration in the blood of uremic patients is about
0,2 g/l, the film adsorber can remove the production of
two days.
When the film adsorber is used simultaneously with a hemo-
dialyser, only a part of the daily production has to be
adsorbed. In that case the adsorption capacity reaches

for the treatment twice a week.

5 the adsorption of albumen
When bovine blood is flown through the film adsorber about
10 g of albumen will be adsorbed until equilibrium is rea-
ched. This equilibrium is reached within two hours, when
the flow rate is 60 ml/min. When the adsorber is flown
previously by a dextran solution the adsorption capacity
for albumen can be halved.

6 the hemolysis in the film adsorber
We found, that the hemolysis caused by the film adsorber
is negligible.
We have not measured the damage to thrombocytes and leu-
kocytes as caused by the film adsorber.

7 the release of particles by the film adsorber
We found no release of any particles by the film adsorber.
This was neither to be expected because of the way of pro-
duction. Nor had it been expected (because of the same
reason) that carbon particles lay bare at the film surface.
This is proven by the pictures of the acc film surface in
paragraph IV-1. The experiment with albumen gives also an
indication in that direction.

8 the competition effect
As was expected with the relatively small concentrations
in blood, we found no competition effect for adsorption.

9 the removal of poisons (other than for cases of renal
   insufficiency)
We have shown, that the film adsorber is an excellent
means to remove barbiturates from blood. Since it has al-
ready been shown by other authors, that also many other
poisons are good adsorbed at activated carbon, it is to be
expected, that the good adsorption of the film adsorber is

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not restricted to barbiturates only.

Also in cases of acute hepatic failure the film adsorber
might be a good assistance for the treatment.

Advantages of the film adsorber are the quick applicabili-
ty and the minimal care needed during the treatment.

10 the simultaneous use of the film adsorber and a dialyser

We have shown, that the film adsorber is a very useful ad-
dition to the dialyser.

Not only the clearances of the molecules with a molecular
weight between 100 and 200 are very much increased, but
especially the removal of the middle molecules is no lon-
ger a restriction for the dialysis treatment.

Since the clearance of urea is not increased, this clea-
rance will fix the time needed for the treatment.

The clearance by the film adsorber is for most solutes
higher than the clearance by the film adsorber. This is a
consequence of the small liquid film thickness of the film
adsorber, the large water content of the acc film, the
small penetration depth (at least at the beginning of the
treatment) and the large exchanging surface.

11 sterilisation of the film adsorber

It is obvious, that no gas sterilisation can be applied.
The materials used in the design of the film adsorber are
able to stand up against steam sterilisation.

We have not looked at sterilisation by means of γ rays. To
us, however, this seems very good possible.

12 optimization of the film adsorber

In our experiments we always used the same dimensions of
the film adsorber. It will be clear, however, that these
dimensions can be chosen at will: the width of the film
(and therewith the length of the roll) can be altered as
well as the number of windings in the roll.

The distance between the windings can be adjusted by

choosing different diameters of the glass beads.

These three parameters (width of the film, number of windings and the spacing between the separate windings) can be used to arrive at optimal conditions in which adsorption capacity, masstransfer rate (or clearance) and pressuredrop are the quantities to be optimized.

Also the materials of the film adsorber can be varied. The glass beads have a bare surface of 140 cm^2 in the total adsorber. It is possible, that this surface causes too much blood damage (platelets). An other material e.g. polystyrene or a polyacrylate can be used.

The same holds for the collodion. An other material can be used. One has, however, to reckon with the way of production.

13 extensions of the film adsorber

As mentioned a film adsorber based only on adsorption at activated carbon, can never totally replace the hemodialyser. The principle of the film adsorber can, however, also be applied to ionexchangers. These ionexchangers might be needed for the removal of urea (the urease might be adsorbed at the ionexchangers), for the removal of NH_4^+ in cases of hepatic failure, but also for the removal of ionic poisons.

The design of the film adsorber can also be used in the hemodialyser with recirculation of the dialysate.

For the total replacement of the dialyser an ultrafiltrator has to be added for the removal of water.

APPENDICES

appendix 1 <u>the analysis of "Merck" activated carbon and</u>
<u>"Ketjen" cracking catalyst</u>

a <u>the carbon</u>

	A % wt	B % wt	C % wt
soluble in water	2	2	
soluble in HCl	8		
Ce	0,01		
SO_4^{--}	0,04	0,035	0
Pb etc	0,005		
Fe	0,01		
Zn	0,001		
loss by drying	8	4,5	

In column A the analysis is shown as given by the manu-
facturer. Column B shows our measurements. To remove the
pollution in the carbon, it was repeatedly washed by water
until the water had no measurable conductivity anymore.
The activated carbon contained no free SO_4^{--} anymore after
this procedure as is seen in column C.
The carbon was washed before experiments examining the ad-
sorption qualities were performed. Some other data are gi-
ven below.

mean particle diameter	40	μm
specific surface	710	cm^2/cm^3 (by BET method)
internal porosity (fraction of empty volume)	0,4	
bulk porosity	0,6	by liquid
density of the solid	1,66 g/cm^3	titration;
density of the particles	1 g/cm^3	Innes (K-1)

b the cracking catalyst

loss by combustion	13,1 %	wet basis
Al_2O_3	24,8 %	wet basis
Na_2O	0,01 %	dry basis
Fe	0,03 %	dry basis
SO_4	0,91 %	dry basis
specific surface	527 m^2/g	
pore volume	0,86 ml/g	
density	0,39 g/ml	

appendix 2 the quantitative analyses

The measurements of the concentrations in experiments, where blood was used (except for the barbiturates) were performed by the clinical laboratorium in the St Jozef hospital in Eindhoven. The concentrations in aqueous solutions were measured with a Carrey 14 recording spectrophotometer.

For each compound described below a standard curve was made (see graph IV-6). A blanco was used as reference. The same cuvet was always used both for the estimated solution and for the blanco.

a creatinine

The creatinine concentration was directly measured at 234 nm.

b inulin

For inulin the concentration was measured at 610 nm after a color reaction following Snell (K-2). 10 ml diphenylamine solution (20% in ethanol) was added to 160 ml of a mixture of ethanol and concentrated HCl (7:5). 1 ml of sample was added to 10 ml of this reagens. The solution is shaken and heated during two hours in water of 80°C.

c albumin

Albumin was measured directly at 210 nm.

d BSP

BSP was measured at 580 nm after dilution with a 20% NaOH
solution.

e barbiturates

5 ml of sample, 0,05 ml buffer (pH=6,8) and 100 ml di-
chloorethane (DCE) were brought in a separation funnel.
After 5 minutes shaking 90% of the DCE was received in a
calibrated cylinder and via a foldered filter added to a
second separation funnel. 5 ml 0,45 N NaOH was added. Af-
ter 5 minutes of shaking the aqueous layer was brought in
a centrifuge tube and centrifugated. 0,33 ml 0,45 N NaOH
was added to 2 ml of extract.

0,33 ml 16% ammonium chloride was added to another 2 ml of
extract. The difference between the extinctions at 320 nm
and 260 nm was used for estimation of the concentration of
barbiturate.

f urea

urea was measured at 420 nm after hydrolysis with urease
and reaction with Nessler reagens.

appendix 3 the correction of the residence time distribu-
           tion curve for the compartments before and af-
           ter the roll

We suppose, that the compartments before and after the
roll are ideal mixers as is mentioned in section III-1-a.
For such a ideal mixer holds:

$$V dC_u/dt = Q(C_u - C_i)$$ (1)

in which

V   is the volume of the ideal mixer

t   is the time

C_u is the concentration in the output of the ideal mixer

C_i is the concentration in the input of the ideal mixer

Q   is the volumetric flowrate

In section III-1-a the measurement of the output concen-

tration of the film adsorber is described. By means of e-
quation (1) the concentration in the output of the roll
can be calculated.

Equation (1) can, however, not be applied for the compart-
ment before the roll, before it is proved, that the se-
quence of the apparatus is of no importance. This prove is
given below.

Suppose we have two apparatus A and B with mean residence
time τ_1 and τ_2 and volumes V_1 and V_2. Before A a pulse δ_1
is given
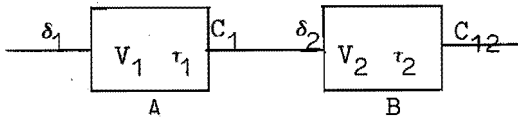
C_1 (the output concentration of A) can be considered as a
serie of pulses before B with a duration of Δt.

At time t_1 the number of pulses between A and B were
$n=t_1/\Delta t$. If $C_1^{\ast}$ is the $C^{\ast}$ of apparatus A, then is the pulse
before B:

$$\delta_2 = Q\Delta t C_1(t_1) = \delta_1 C_1^{\ast}(t_1)\Delta t/\tau_1 \tag{2}$$

If $C_2^{\ast}$ is the $C^{\ast}$ diagram of B then at time t' after the in-
jection of δ_2:

$$C_{12}'(t'+t_1) = \delta_2 C_2^{\ast}(t')/V_2 \tag{3}$$

If $t' + t_1 = t_2$ then

$$C_{12}'(t_2) = \delta_2(t_1)C_2^{\ast}(t_2-t_1)/V_2 \tag{4}$$

The real concentration C_{12} is the sum of all concentra-
tions C_{12}' owing to the serie of pulses:

$$C_{12}(t_2)=\sum C_{12}'(t_2)=\sum \delta_1 C_1^{\ast}(t_1)C_2(t_2-t_1)\Delta t/V_2\tau_1 \tag{5}$$

If t_2 is constant, t_1 can vary between 0 and t_2 and the
summation is therefore between 0 and $t_2/\Delta t$. For $\Delta t \to 0$:

$$C_{12}(t_2)=(\delta/V_2\tau_1)\int_0^{t_2}C_1^{\ast}(t_1)C_2^{\ast}(t_2-t_1)dt_1 \tag{6}$$

or

$$C_{12}^{\textbf{x}}(t_2)=((\tau_1+\tau_2)/\tau_1\tau_2)\int_0^{t_2}C_1^{\textbf{x}}(t_1)C_2^{\textbf{x}}(t_2-t_1)dt_1 \qquad (7)$$

From this result follows, that $C_{12}^{\textbf{x}}$ does not change, if the sequence of A and B is changed. If $t_{11} = t_2 - t_1$ is substituted, follows:

$$C_{12}^{\textbf{x}}(t_2)=((\tau_1+\tau_2)/\tau_1\tau_2\int_0^{t_2}C_1^{\textbf{x}}(t_2-t_{11})C_2^{\textbf{x}}(t_{11})dt_{11} \qquad (8)$$

Equation (1) can thus be applied even if the ideal mixer is placed before the roll.

appendix 4 the calculation of the diffusion coefficient
from the measurements with the SMDC

V_u and V_l are ideal mixers separated by a membrane and with the concentrations C_u and C_l. For the change of C_b with time holds:

$$V_u dC_u/dt = kA_m(C_l-C_u) \qquad (1)$$

in which

V_u is the volume of the upper compartment
C_u is the concentration in the upper compartment
C_l is the concentration in the lower compartment
k is the mass transfer coefficient
A_m is the membrane surface

A mass balance over the whole SMDC renders

$$V_l C_l + V_u C_u = V_l C_{li} + V_u C_{ui} \qquad (2)$$

in which C_{li} and C_{ui} are the initial concentrations. Elimination of C_l out of (1) and (2) renders after integration

$$\ln\frac{C_{li}-C_{ui}}{(C_l-C_u)_{t_1}} = kA_m t_1(1/V_l+1/V_{u1}) \qquad (3)$$

By the sampling V_u is reduced, which required a correction For integration from $t_1 \rightarrow t_2$ holds:

$$\ln\frac{(C_l-C_u)_{t1}}{(C_l-C_u)_{t2}} = kA_m(t_2-t_1)(1/V_l+1/V_{u2}) \qquad (4)$$

From $0 \to t_2$ (3) and (4) have to be added

$$\ln\frac{(C_1-C_u)_{t0}}{(C_1-C_u)_{t2}} = kA_m[t_1(1/V_{u1}-1/V_{u2})+t_2(1/V_1+1/V_{u2})] \quad (5)$$

and in general from $0 \to t_i$:

$$\ln\frac{(C_1-C_u)_{t0}}{(C_1-C_u)_{ti}} = kA_m\left\{\sum_0^{i-1}[t_n(1/V_{un}-1/V_{un+1})] + \right.$$
$$\left. + t_i(1/V_1+1/V_{ui})\right\} = kA_mf(t_i,V_{ui}) \quad (6)$$

The term with the addition sign is the correction factor for the sampling. If one plottes $f(t_i,V_{ui})$ against

$$\ln\frac{(C_1-C_u)_{t0}}{(C_1-C_u)_{ti}}$$

the slope of the line will be kA_m. k can be calculated from kA_m and D can be calculated from $k=D/\delta$ in which δ is the thickness of the film.

appendix 5 <u>the criterium of Taylor for a flow between parallel planes</u>

The convective diffusion equation for a flow between two parallel planes can be described by the following equation

$$\delta C/\delta t = D(\delta^2C/\delta x^2+\delta^2C/\delta y^2) - v_x\delta C/\delta y \quad (1)$$

The velocity at point x is

$$v_x = 6\bar{v}(x/d-x^2/d^2) \quad (2)$$

We choose a coordinate system with a velocity $\bar{v}$ so that

$$v_x = 6\bar{v}(x/d-x^2/d^2) - \bar{v} \quad (3)$$

Suppose the axial concentration change is much smaller than the radial change: $(\delta^2C/\delta y^2) = 0$

$$\delta C/\delta t = D\delta^2C/\delta x^2 - \bar{v}(6x/d-6x^2/d^2-1)\delta C/\delta y \quad (4)$$

Suppose $\delta C/\delta t = 0$ and if $\delta\bar{C}/\delta y$ is independent of x and the following boundary conditions could be applied

$$(\delta C/\delta x)_{x=0} = 0 \quad \text{and} \quad x=\tfrac{1}{2}d: \ C=C_o$$

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then is the solution of (4):

$$C=C_o+(\bar{v}d^2/D)(x^3/d^3-\tfrac{1}{2}x^4/d^4-\tfrac{1}{2}x^2/d^2+1/32)\delta\bar{C}/\delta y \qquad (5)$$

The mean concentration over the cross section (not the cup mixing concentration) is:

$$\bar{C}=\int_0^d Cdx \ /d=(\bar{v}d^2/D)(1/32-1/60)\delta\bar{C}/\delta y + C_o \qquad (6)$$

then
$$C=\bar{C}+(\bar{v}d^2/D)(x^3/d^3-\tfrac{1}{2}x^4/d^4-\tfrac{1}{2}x^2/d^2+1/60)\delta\bar{C}/\delta y \qquad (7)$$

The flux is

$$j=Q/d=[\int_0^d Cvdx]/d=-0,01(\bar{v}d^2/D)\delta\bar{C}/\delta y=-D_{eff}\delta C/\delta y \qquad (8)$$

We can now describe the masstransport by means of an effective diffusion coefficient if

$$D\ll D_{eff} \quad \text{or} \quad \bar{v}d/D\gg 10 \qquad (9)$$

If $\delta C/\delta y$ is nearly constant follows after differentation of (7)

$$\delta C/\delta y = \delta\bar{C}/\delta y + (d^2\bar{v}/4D)(-1/60+\tfrac{1}{2}x^4/d^4-x^3/d^3 +$$
$$+ \tfrac{1}{2}x^2/d^2)\delta^2C/\delta y^2 \approx \delta\bar{C}/\delta y \qquad (10)$$

if
$$\delta\bar{C}/\delta y \gg (\bar{v}d^2/D)(\delta^2C/\delta y^2) \qquad (11)$$

If L is the length over which a change in C appears then
$$LD/\bar{v}d^2 \gg 1 \qquad (12)$$

or with(9)
$$LD/\bar{v}d^2 \gg 10 \qquad (13)$$

If this criterium holds, a flow through a slit can be described by a Poisseuille flow with radial diffusion.

Appendix 6 <u>the pressuredrop velocity relation with the assumption of a marginal plasma layer along the walls of the channel</u>

From the Casson relation:
$$\tau^{\tfrac{1}{2}} = \tau_o^{\tfrac{1}{2}} + \eta_s\gamma^{\tfrac{1}{2}} \qquad (1)$$

Merill (I-7) and Kooyman (I-5) have derived the following

relation between the pressuredrop and the velocity:

$$3\bar{v}\eta_s/a\tau_o = \tau_D - 12\tau_D^{\frac{1}{2}}/5 + 3/2 - \tau_D^{-2}/10 \qquad (2)$$

Assuming a marginal plasma layer Charm and Kurland (I-8) derived a similar relation for a blood flow through a capillar. For a flow between two parallel planes we derived the relation between the pressuredrop and the velocity as follows.

From equation (1) follows for a blood flow between two parallel planes with a distance 2a for the velocity gradient at a point y in the channel:

$$\gamma = dv/dy = (\tau - 2\tau^{\frac{1}{2}}\tau_o^{\frac{1}{2}} + \tau_o)/\eta_s \qquad (3)$$

The coordinate system is relative to the centre plane between the parallel planes

$$\tau = y\Delta p/L \qquad (4)$$

Substitution of (4) in (3) and integration over the channel gives for the plasma layer:

$$1 < \xi < (a-\varepsilon)/a = \Delta$$
$$\eta_s v/a\tau_o = \eta_s \tau_D(1-\Delta^2)/2\eta_p \qquad (5)$$

and for the blood layer:

$$\Delta < \xi < \tau_D^{-1}$$
$$\eta_s v/a\tau_o = \tfrac{1}{2}\tau_D(\Delta^2-\xi^2) - 4\tau_D^{\frac{1}{2}}(\Delta^{3/2}-\xi^{3/2})/3 +$$
$$+ (\Delta-\xi) + \eta_s(1-\Delta^2)/2\eta_p \qquad (6)$$

and $\quad \tau_D^{-1} \leqq \xi < 0$
$$\eta_s v/a\tau_o = \tfrac{1}{2}\tau_D(\tfrac{1}{2}\Delta^2-\tau_D^{-2}) - 4\tau_D^{\frac{1}{2}}(\Delta^{3/2}-\tau_D^{-3/2})/3 +$$
$$+ (\Delta-\tau_D^{-1}) + \eta_s\tau_D(1-\Delta^2)/2\eta_p \qquad (7)$$

$\tau_D = \tau_w/\tau_o$ in which τ_w is the shear stress at the wall and $\xi = y/a$.

Integration of the equations (5), (6) and (7) over the total cross section of the channel gives for the mean velocity

$$3\eta_s\bar{v}/a\tau_o = \tau_D (1-\Delta^3)/1-\alpha\varphi)+\Delta^3 -$$
$$-12\Delta^{3/2}\tau_D^{\frac{1}{2}}/5 + \tfrac{1}{2}\Delta^2 \qquad (8)$$

This equation is used in section III-1-d2c for the comparison with the measured values of Δp and $\bar{v}$.

Appendix 7 <u>some data about barbiturates</u>

Barbiturates are derivatives of barbituric acid. They are used as sedatives.
For normal men the hypnotic dose is 0,2-0,1 g of phenobarbital and 0,1 g of secobarbital.
Commercial names for phenobarbital and secobarbital are respectively luminal and seconal.
The rate of removal of a barbiturate from the body is not only a function of the clearance of the used apparatus, but is also fixed by the adsorption of the barbiturates by plasma proteins and by the solubility of the barbiturates in the cells of the body.
By Goldbaum (J-7) was found, that phenobarbital is adsorbed for 20 % at the proteins in the plasma and secobarbital for 44 %. These values are not fixed but are depending among others on the barbiturate concentration, but these values are the most normal.

SYMBOLS

A	total exchanging surface	m^2
a	half of the thickness of the liquid film	μ
	specific surface area	m^{-1}
α	correction factor in the formula of Einstein (III-1-10)	
b	breadth of the liquid film; length of the acc film	m
C	concentration	g/l
$C^{\divideontimes}$	concentration in equilibrium with the solid phase concentration: $C^{\divideontimes}=mq$	g/l
C^{+}	Laplace transformation of C	
Cl	clearance	ml/min
$\Delta C_{\log}$	logarithmic averaged concentration difference	g/l
γ	shear rate	sec^{-1}
D	dialysance	ml/min
	diffusion coefficient	m^2/sec
d	film thickness	μ
	diameter	m
δ	thickness of the marginal plasma layer	μ
	amount of pulse injection	g
Δ	dimensionless plasma layer thickness	
e	$\epsilon_i(1-\epsilon_e)/\epsilon_e$	
ϵ	porosity; ϵ_i=internal porosity; ϵ_e=external	
η	viscosity	$Nsec/m^2$
Θ	time modulus	
F	$\sum C\Delta t$ for the RTD measurement	gsec/l
g_c	volume amount of carbon	g
K	exchange coefficient	sec^{-1}
k	masstransfer coefficient	m/sec
k_o	overall masstransfer coefficient	m/sec
L	length of the slit; breadth of the acc film	m
M	molecular weight	g/mol
m	equilibrium coefficient	

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μ_1	first moment	sec
μ_2	second moment	sec^2
N_L	number of transfer units of an apparatus	
N_z	dimensionless length of an adsorber	
n	velocity of rotation	rev/sec
Δp	pressuredrop	N/m^2
φ	volume fraction of blood cells	
Φ	masstransfer rate	g/sec
Q	volumetric flowrate	m^3/sec
q	adsorbed quantity	g/g_c
R	inner radius of the film adsorber	cm
	half of the thickness of the acc film	μ
r	radius	m
ρ	density	kg/m^3
Sh	Sherwood number	
T	temperature	^oK
t	time	sec
τ	shear stress	N/m^2
	mean residence time	sec
τ_o	yield value	N/m^2
τ_D	dimensionless shear stress: $a\Delta p/\tau_o L$	
V	volume	m^3
v	velocity	m/sec
$\bar{v}$	mean velocity	m/sec
v_o	superficial velocity	m/sec
X	dimensionless concentration	
x	correction factor in the formula of Wilke and Chang (III-2-1)	
Y	dimensionless adsorbed quantity	
Z	throughput parameter	

subscripta

b blood

c carbon

d dialyser or dialysate

f acc film or film adsorber

i input

l liquid film
  lower compartment of the SMDC

m membrane

o output

p plasma

s serum or stirrer

t total

u upper compartment of the SMDC

w water

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J. the adsorption of barbiturates

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tasaio   Trans of the Am Soc for Art Int Organs
edta   Europ Dialysis and Transplant Association

STELLINGEN

1 De waarden, die voor de plasmaeiwitbinding van barbitura-
ten gegeven zijn door Goodman (1), geven slechts een in-
druk van de onderlinge verhoudingen van de sterkte van de
eiwitbindingen der barbituraten, maar niet van de absolu-
te grootte van de binding (zie Goldbaum (2)).

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2 Voor gefluidiseerde bedden is het zinloos om de stof- of
warmteoverdracht van het doorstromende gas naar de geflui-
diseerde deeltjes weer te geven in een Chilton-Colburn
factor, zolang aan het bestaan van bellen voorbij gegaan
wordt (zie Gupta (3) en Inazumi (4)).

   (3) Gupta SN et al "Fluid-particle heat transfer in fixed
      and fluidized beds" Chem Eng Sci 29 (1974) 839.

   (4) Inazumi H et al "Dehumidification of moist air in a
      fluidised bed" Int Chem Eng no4 14 (1974) 768.

3 Uit eigen onderzoek (v.Zutphen (5)) blijkt, dat door ad-
sorptie van urease aan aluminium-silicium oxides de akti-
viteit van dit enzym vergroot wordt. Een voorafgaande be-
handeling van de oxides met een verdund zuur vergroot de-
ze aktiviteit nog meer.

   (5) v.Zutphen P "De hydrolyse van ureum met behulp van
      urease" intern rapport THE.

4 Het verdient aanbeveling indien bij het doen van verblijf-
tijdspreidings metingen meer aandacht wordt geschonken aan
mogelijke fouten in meettechniek zoals beschreven door
White (6).

(6) White ET "Sources of error in the measurement of resi-
dence time distribution" J Imp Coll Chem Eng Soc
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5 Het vermoeden van Ikkenberry (7), dat voor een membraan
geldt, dat de logarithme van de permeabiliteit omgekeerd
evenredig is met het waterpercentage van het membraan is
door eigen metingen bevestigd.

(7) Ikkenberry Ld et al "Characterization of membrane ma-
terials for hemodialysis" Chem Eng Progr Symp Ser
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6 Uit de adsorptieproeven van Gazzard (8) aan tot microcap-
sules verwerkte aktieve kool kan berekend worden, dat
zelfs bij verwerking met behulp van 10 gewichtsprocent
aan polymeer nog 5 % van het aktieve koolopppervlak onbe-
dekt blijft.

(8) Gazzard BG et al "Polymer coating of activated char-
coal and its effect on biocompatibility and parace-
tamol binding" Clin Sci and Mol Med 47 (1974) 97.

7 De stofoverdracht naar een starre bol wordt in geval van
een constante grensvlakconcentratie bij een Fouriertijd
(Dt/d^2) groter dan 0,05 bepaald door de inwendige diffusie
en kan beschreven worden door Sh=6,6 (zie o.a. Thijssen
(9)). De starre bol is dan echter al voor 65 % verzadigd.

(9) Thijssen HAC et al "Stofoverdrachtsprocessen" college-
diktaat THE 1973.

8 Aangezien de stoffen die uit bloed verwijderd moeten wor-
den in geval van leverbeschadiging zowel van organische
als van ionogene aard zijn zal de hemoperfusie over
ionenwisselaars of over aktieve kool afzonderlijk niet
voldoende zijn, maar moet aan een combinatie van deze ad-
sorbentia gedacht worden.

9 Het is onbegrijpelijk, dat naast de evolutietheorie van
Darwin de rampentheorie van Velikowski (10 en 11) nog
niet geaccepteerd wordt.
  (10) Velikowski I "Worlds in collision" Sphere books Ltd
       1972.
  (11) Velikowski I "Earth in upheavel" Doubleday & compa-
       ny Ltd New York.

10 Het voordeel van de bridgesport boven andere denksporten
is, dat een wedstrijd uit meerdere spellen bestaat en dat
dus één blunder niet een hele middag denksporten in het
water gooit.

26-09-1975   P.v. Zutphen