DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 14(15-17), 2625-2630 (1988)

A CONTRIBUTION TO TRANSFER OF MATTER THROUGH A POLYMER MEMBRANE

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Controlled release of the active ingredient from a drug delivery system may be obtained by means of an enclosure (wall) consisting of a permeable polymer membrane. When creating similar drug delivery systems, prior selection of the film-forming material is unavoidable. From physical viewpoints, the most important film property in such selection is its coefficient of permeation P. This property can within the scope of preformulation studies be followed in the system model membrane - drug (either real or model one).

EXPERIMENTAL

Membranes were prepared by a routinely used method from pure ethylcellulose, and ethylcellulose with added polyethylene glycol 4000. Methylene blue in aqueous solution has been used as model permeating matter. The permeation rate was followed using the Sartorius Absorption Simulator instrument (Fig. 1). This equipment consists of two separate compartments, the donor and the acceptor ones, with the studied membrane positioned between them. The compartment contents are being mixed, with a pump ensuring circulation of the solution. Samples are taken in certain time periods to determine the concentration of permeated matter. The concentration of the methy-

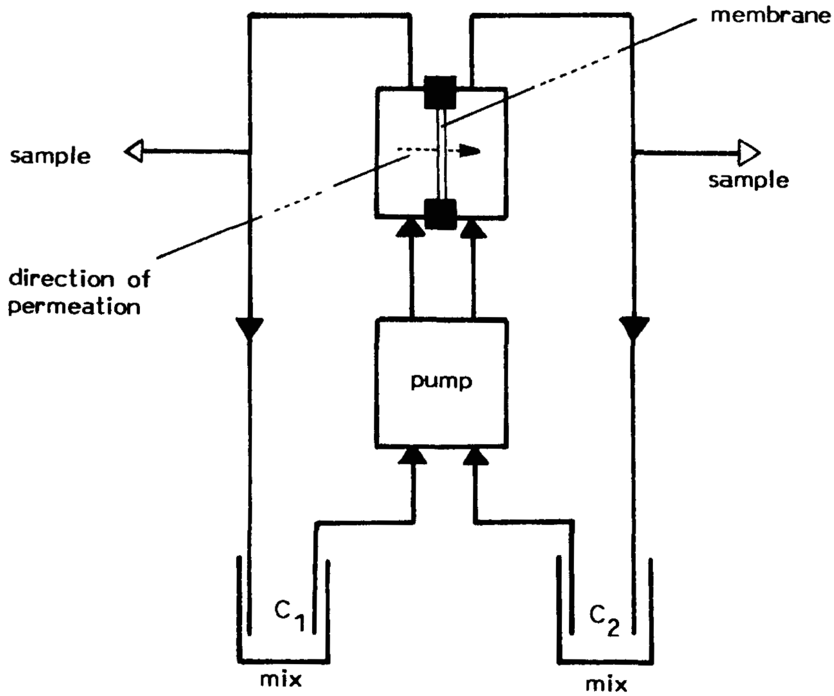

FIGURE 1

Sartorius Absorption Simulator Instrument

$c_1 > c_2$

lene blue has been determined by measurement using Spekol 11 spectrophotometer (Carl Zeiss, Jena).

Physico-Mathematical Description

Rate of permeation through a membrane is described by the equation :

$$\frac{dc_2}{dt} = \frac{PA}{hV} (c_1 - c_2) \qquad (1)$$

where V is the solution volume in individual compartments, A is the membrane area, h its thickness, and P the permeation coefficient, with the following relationship being valid at all times :

$$c_1 + c_2 = c_o = \text{const.} \qquad (2)$$

If concentrations are being determined by means of a flow analysator (ie. no solution is being taken off the system) or in the case when the samples are returned immediately after analyzing them into the system, then from Equation (1) the following relationship can be derived for the time dependence of concentration c_2 :

$$c_2 = \frac{c_o}{2}\left[1 - \exp\left(-\frac{2PA}{hV}\,t\right)\right] \qquad (3)$$

If samples cannot be returned into the system, then Eqution (1) cannot be used for the entire duration of the experiment but only for a small time interval $t_i - t_{i+1}$ between two consecutive sample offtakes :

$$\left[\frac{dc_2}{dt}\right]_i = \frac{PA}{h(V - iv)}\,(c_o - 2c_2) \qquad (4)$$

where v is the sample volume. To avoid a complex analysis, Equation (4) results, for the entire time range[1], in

$$c_{2i} = \frac{c_o}{2}\left[1 - \exp\left(\frac{2PA}{h}\,Z_i\right)\right] \qquad (5)$$

where

$$Z_o = 0 \qquad t_o = 0 \qquad (6)$$

$$Z_i = Z_{i-1} - \frac{t_i - t_{i-1}}{V - (i-1)v} \qquad (7)$$

$$i = 1, 2, 3, \ldots, n$$

By regression of the experimental data $c_2 = f(t)$ according to the functions (3) or (5), the coefficient of permeation P can be determined. For the second sampling method, (ie. regression by Equation (5)) the respective calculating program in BASIC-G language is presented as implemented by the PMD 85 and PMD 85-2 microcomputers.

RESULTS

The application of the regression function (5) and the BASIC program shall now be illustrated by means of results obtained with two kinds of membranes :

A/ Ethyl cellulose : polyethylene glycol ratio 5 : 1 , thickness 74 µm, area 40 cm^2

B/ Ethyl cellulose : polyethylene glycol ratio 5 : 5 , thickness 88 µm, area 40 cm^2.

Compartment content volumes (in both cases) : 100 ml, sample volumes 3 ml, initial concentration $c_1 = 3\ mg.ml^{-1}$.

The diagram (Fig. 2) shows that both experimental and regression data are congruent. The permeation coefficient values obtained are as follows :

$$P_A = 1.61 \times 10^{-9}\ cm^2.\ s^{-1}$$

$$P_B = 1.54 \times 10^{-8}\ cm^2.\ s^{-1}$$

BASIC-G Program

```
10 REM   COEFFICIENT OF PERMEATION
20 REM   sampling method 2
30 GCLEAR
40 DIM T(50) : DIM C(50) : DIM Z(50)
50 READ N
60 FOR I=1 TO N
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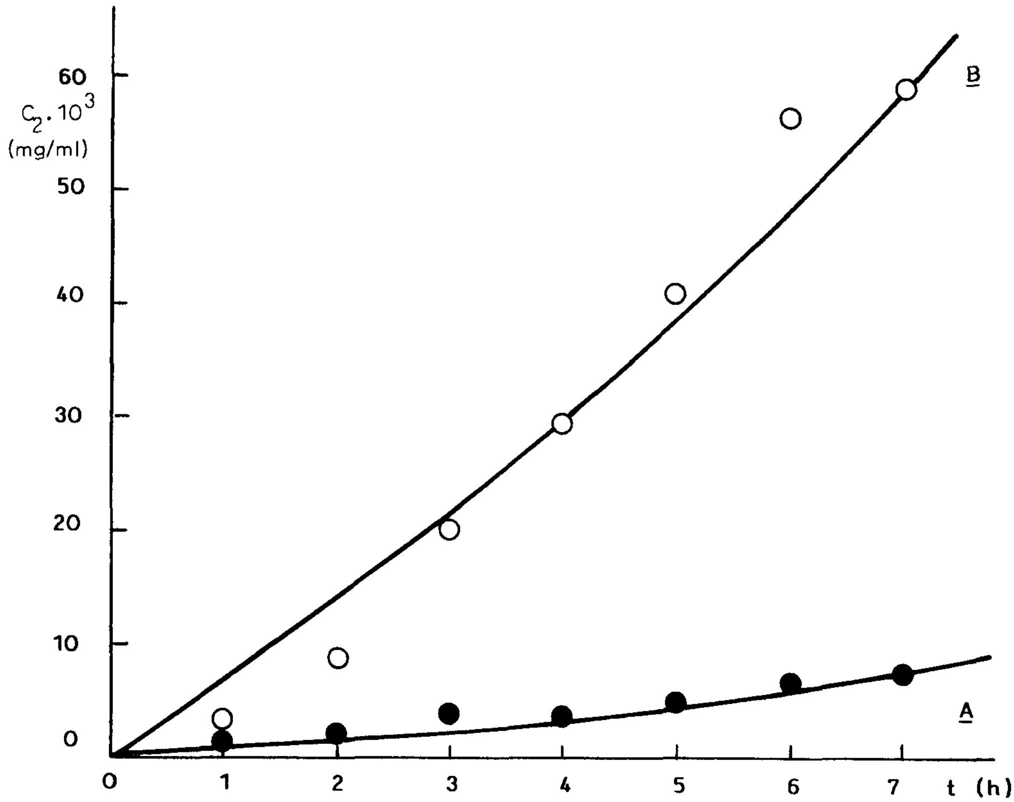

FIGURE 2

Permeation of Methylene Blue through Composite Membranes

A and B

(experimental and regression values)

```
7Ø  READ T(I),C(I): T(I)=3600×T(I)
8Ø  NEXT I
9Ø  V=1ØØ
1ØØ PRINT "ENTER h": INPUT H:  REM film thickness
11Ø PRINT "ENTER A": INPUT A:  REM membrane surface area
12Ø PRINT "ENTER V": INPUT V:  REM compartment volumes
13Ø PRINT "ENTER v": INPUT VV:  REM sample volume
14Ø PRINT "ENTER CØ": INPUT CØ: REM C1+C2
15Ø ZL=Ø : ZZ=Ø
16Ø Z(1)=Ø
17Ø FOR I=2 TO N
18Ø Z(I)=Z(I-1)-(T(I)-T(I-1))/(V-(I-1)×VV)
19Ø NEXT I
2ØØ FOR I=2 TO N
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```
210 ZL=ZL+Z(I)×LOG(1-2×C(I)/C0)
220 ZZ=ZZ+Z(I)×Z(I)
230 NEXT I
240 P=(H/(2×A))×(ZL/ZZ)
250 FOR I=2 TO N
260 PRINT  (1-EXP(2×P×A×Z(I)/H))×C0/2
270 NEXT I :  REM regression values C(I)
280 AA=0 : AV=0 : AR=0
290 FOR I=2 TO N
300 AA=AA+C(I)
310 NEXT I
315 AN=AA/(N-1)
320 FOR I=2 TO N
330 AV=AV+(C(I)-AN)×(C(I)-AN)
340 AR=AR+(C(I)-(1-EXP(2×P×A×Z(I)/H))×C0/2)×(C(I)-(1-EXP(2×P×A×Z(I)/H))×C0/2)
350 NEXT I
360 S2=(AR/(N-2))
370 S1=SQR(S2)
380 IK=SQR(1-AR/AV)
390 PRINT "ss=" ; S2:  REM  residual regression dispersion
400 PRINT "s =";  S1:  REM  standard deviation of regression
410 PRINT "i =";  IK:  REM  correlation index
420 PRINT "P =";  P:   REM  coefficient of permeation
500 DATA 8,0,0,1,.99,2,2.32,3,3.7,4,3.49,5,5,6,6.62,7,7.33
600 END
```

The following units are to be used as input data : cm, cm^2, cm^3 (or ml, respectively) ; time h ; concentration C(I) and C0 - an arbitrary but consistently used unit of quantity per cm^3 (ml). Then, the P value shall be expressed in $cm^2 . s^{-1}$ units.

CONCLUSIONS

The physico-mathematical description of experimental determination of the permeation coefficient for the model system of membrane-transferred matter as well as the BASIC-G program designed for the calculation of the permeation coefficient within this system based on experimental data obtained by the SARTORIUS ABSORPTION SIMULATOR instrument are presented.

REFERENCES

1. Zs. Szentirmai, G. Hortobagyi and I. Kolbe, Acta Pharm. Hung. 50, 212 (1980).