Accelerated Removal of Salicylate by Additives in Peritoneal Dialysis Fluid

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Abstract □ A variety of compounds was tested for effect on peritoneal dialysis of salicylate. They were compared by means of apparent rate constants obtained *via* analysis of plasma and dialysate curves with an analog computer. One combination of substances, anthranilic acid 1% and *N*-myristyl-β-aminopropionate 0.25%, was selected as most promising. This combination was tested by intermittent dialysis and shown to remove about three times as much salicylate as the control fluid.

Keyphrases □ Peritoneal dialysis—acceleration, additives □ Salicylate, ^{14}C-tagged—dialysis removal □ Anthranilic acid–*N*-myristyl-β-aminopropionate—dialysis acceleration □ Scintillometry—analysis

Salicylate is the drug most frequently encountered in accidental poisonings, and effective means for its removal in such cases is of paramount importance. Peritoneal dialysis is one method frequently used, though removal by this route is slow. Thus, a means of accelerating this process has been sought and is the topic of this paper.

Other workers have achieved some success in accelerating salicylate dialysis *via* substances added to the dialysis fluid. Nahas *et al.* (1) used THAM [tris(hydroxymethyl)aminomethane] and bicarbonate with the aim of maintaining a maximum concentration gradient *via* high pH in the peritoneal fluid. Their tests with dogs gave 1.3 times as much removed with THAM and 1.6 times as much with bicarbonate as with control fluid. Etteldorf *et al.* (2) used 5% albumin and pooled serum on dogs to remove about 1.5 times as much salicylate as with control. Similar results were obtained by James *et al.* (3).

In this study a wide variety of substances was tested for possible accelerating effects. A number of wetting agents and detergents were tested, since previous work had shown such materials to promote dialysis of urea (4). Several organic compounds of structure similar to salicylate were tested with the aim of displacing salicylate from tissue-binding sites. Drugs which might affect microcirculation in the mesentery by one mechanism or another were included. ATP-ase-blocking agents and calcium-binding agents were evaluated in the hope of increasing membrane permeability. The test compounds were used in concentrations as high as practicable, taking into consideration toxicity, osmotic pressure effects, and reduction of blood pressure which might make sampling of blood and urine difficult.

An *in vitro* dialysis test was used to evaluate the compounds, this being quite similar to the procedure used with urea dialysis (4). Substances were compared by means of apparent rate constants and those which had significant accelerating action were studied in greater detail. Finally, the one combination of compounds selected as most promising was tested by intermittent dialysis to simulate results to be expected in a clinical procedure.

EXPERIMENTAL

Dialysis Screening Test—Male albino rabbits were used as the test animal and an intravenous dose of 100 mg./kg. of ^{14}C-tagged salicylate was administered. A 30-min. period was allowed for distribution throughout the body fluids and then 150 ml. of dialysis fluid was injected intraperitoneally *via* an infant-size peritoneal catheter. At intervals of about 10 min. samples of blood and dialysis fluid were obtained over a period of 160–180 min. At the same time the urine was collected by means of a catheter. Urine data, not used for the analysis and not included in this report, was examined to detect any significant changes in excretion rate which might be caused by the test compounds, but none was observed. The samples of plasma and dialysis fluid were counted in a liquid scintillation counter as previously described (4) except that the counting fluid consisted of POPOP 0.01% and PPO 0.4% in a solvent of 33% nonionic surfactant,[1] 67% toluene. Results were calculated in terms of salicylate concentration.

The model for this system may be expressed as follows:

$$\begin{array}{ccc} & & k_1 f \\ & 1 & \rightleftarrows 2 \\ k_3 & \downarrow & k_2 \\ & 3 & \end{array} \qquad \text{(Model 1)}$$

where Compartment 1 is the plasma and equivalent body fluid, 2 is the dialysate, and 3 is the urine. The constant $k_1 f$ is the apparent rate constant describing flow from 1 to 2, where k_1 is the first-order constant for dialysis of free drug and f is the fraction of total drug which is not protein-bound. There is no convenient way to separate k_1 and f, since protein binding is different in plasma and the other body fluids and since the drugs tested may affect protein binding to a variable degree as the experiment proceeds. The combined constant, $k_1 f$, was quite satisfactory for this purpose, however, reflecting the overall transport rate without regard for mechanism. The constant expressing transport from dialysate back to the plasma, k_2, may not be expected to be identical to k_1, since an unknown amount of transport occurs from the peritoneum to the blood *via* the lymph, yet it may be taken as an approximation of k_1 for this purpose. With this assumption, the ratio of $k_1 f/k_2$ yields an estimate of f, the fraction of free drug. Thus, from values of $k_1 f$ and k_2 one can compare various compounds as to their effect on transport rate across the membrane and their effect in freeing the salicylate from protein attachment. It is conceivable that a drug might double the transport rate but increase the protein binding and yield no improvement in removal of salicylate; another might have no effect on transport rate constant but free the salicylate from binding sites and thus be quite useful in removing salicylate from the body. Both mechanisms of action are of interest and thus both $k_1 f$ and k_2 estimates were obtained.

The data were analyzed using concentrations in plasma and dialysate rather than amounts, in this way avoiding the errors inherent in using average or estimated values for distribution volume of the drug The differential equation:

$$\frac{dX_2}{dt} = k_1 f X_1 - k_2 X_2 \qquad \text{(Eq. 1)}$$

was used for the analysis, X_1 being plasma concentration, X_2

[1] Triton X-100, Rohm & Haas, Philadelphia, Pa.

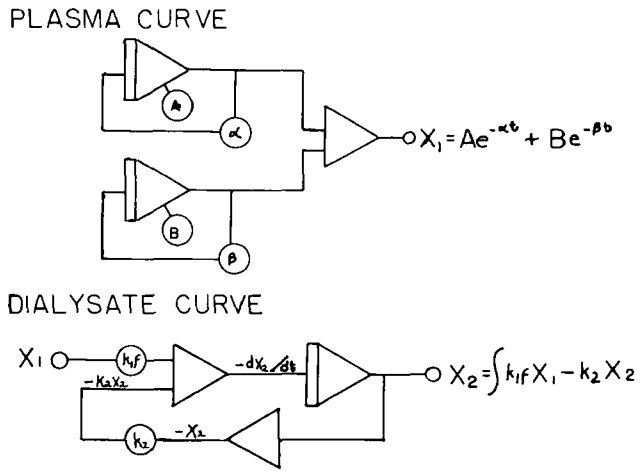

Figure 1—*Diagram of analog computer program for obtaining* $k_1 f$ *and* k_2 *values.*

dialysate concentration. Graphs of the plasma and dialysate experimental points were plotted as a function of time and an analog computer was adjusted to describe the blood curve by a double exponential decay program. The blood concentration function in the computer was then fed to the program integrating Eq. 1, yielding values of $k_1 f$ and k_2. The computer program is diagrammed in Fig. 1.

At the beginning of this study the separation of metabolites from plasma and dialysis fluid was performed with a number of experiments. The extraction method of Brodie *et al.* (5) was found not to give complete extraction of salicylate added to plasma or dialysis fluid as evaluated by liquid scintillation counting, so a method was developed which gave complete transfer of radioactivity. This procedure was as follows.

To 0.5 ml. of plasma or dialysis fluid add 0.1 ml. concentrated hydrochloric acid and 0.5 ml. ethanol and mix. Chill and centrifuge to remove precipitated proteins and salts. Transfer the clear centrifugate to a suitable vial, washing the precipitate once with cold ethanol and adding the washing to the same vial. Evaporate the ethanol solution to dryness on a freeze drier. Add 0.1 ml. of pyridine to the residue and mix to dissolve the organic materials and leave the bulk of the salts undissolved. Transfer a portion of the pyridine solution to a cellulose-backed silica thin-layer chromatographic sheet. Develop the chromatograph in benzene–acetic acid–water (40 : 40 : 20) allowing only the benzene layer to contact the chromatographic sheet (6). Locate the spots under UV light, cut them from the sheet, and measure the radioactivity of each spot. Calculate the fraction of unchanged drug present and apply this fraction to an independent count of the original fluid to obtain the concentration of unchanged drug in the sample.

It was found that with the 3-hr. experiments, the amount of metabolite in plasma and dialysate was 2 to 7% of the total and never exceeded 7%. Higher amounts of metabolite appeared in urine, indicating that the rapid clearance of metabolite by the kidney prevented accumulation of the metabolic products in plasma and dialysate. Similarly, the plasma of man has been found nearly free of salicylate metabolites due to their rapid excretion (7). It was concluded that the fraction of counts representing metabolite in plasma and dialysate was negligible and only total counts were used.

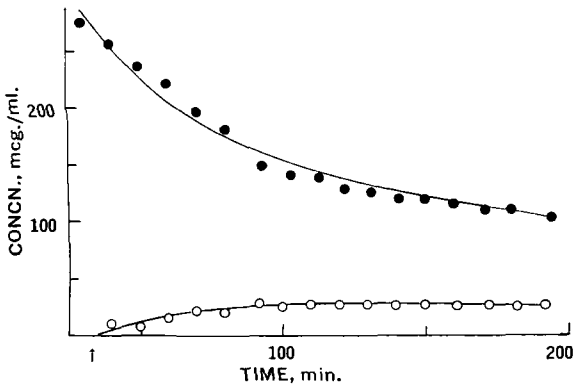

Figure 2—*Typical plasma and dialysate curves for salicylate dialysis with control fluid. Lines are computer-drawn. Key:* ●, *plasma;* ○, *dialysate.*

Intermittent Dialysis—Intermittent dialysis was performed with an i.v. dosage of salicylate of 100 mg./kg. and the volume of dialysis fluid in each exchange was 60 ml./kg. In this test 60 min. was allowed for stabilization of the blood curve prior to introduction of the first dialysis fluid, thus affording average blood levels for the first dialysis period at a point where the blood curve has less curvature. The first fluid was allowed to remain in the peritoneum for 30 min. at which time drainage was started. Ten minutes was allowed for drainage in every exchange. Second and subsequent peritoneal fluids were left in the peritoneum for 19 min. each. One minute was used in each instance to introduce the fluid by means of a large syringe attached to the peritoneal catheter. For clearance calculations the dwell time used for the first exchange was considered as 35 min., for the others. 24 min., thus including half the drainage time as exposure time. Five exchanges were conducted with each animal.

Blood and urine samples were taken at the time of introduction of the first dialysis fluid and at the time drainage was started with each fluid. Dialysis fluid was drained into a graduated cylinder, its volume was measured, it was then poured into a suitable stoppered bottle, and thoroughly mixed prior to removal of a sample for assay. Measurement was by scintillation counting as before.

Intermittent dialysis results were calculated in terms of percent of dose removed in the dialysate and in clearance values based on average blood level in the period of exchange.

Dialysis Fluids—In all tests the dialysis fluids were made isotonic with standard 1.5% dextrose formulas,[2] 377 mosm/l. In most instances this was achieved by diluting the test substance in water to obtain equivalent osmolarity and adding control dialysis fluid to volume. In this manner the concentrations of sodium, calcium, magnesium, and lactate were kept as close as possible to the control formula.

RESULTS

Results of dialysis screening tests are shown in terms of apparent rate constants, $k_1 f$ and k_2, in Table I. Each entry in the table represents a single animal. Figures 2 and 3 illustrate typical plasma and dialysate curves for a control and an effective dialysis accelerator fluid.

It is seen from Table I that although a number of compounds had some accelerating effect on salicylate dialysis, few had a consistent effect. Both anthranilic acid and *N*-myristyl-β-aminopropionic acid[3] accelerated dialysis and the difference in their structures makes it

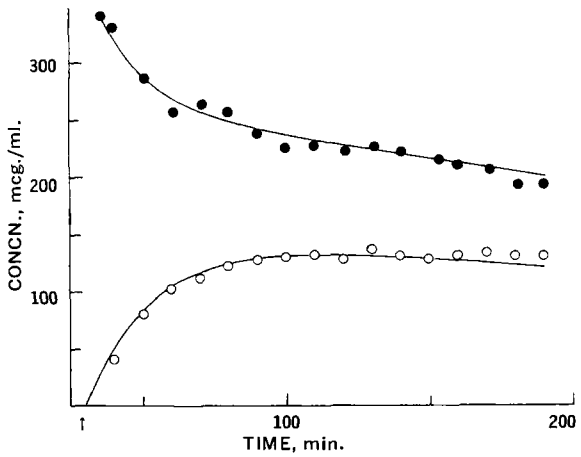

Figure 3—*Typical plasma and dialysate curves for salicylate dialysis with M-1 fluid. Lines are computer-drawn. Key:* ●, *plasma;* ○, *dialysate.*

[2] Inpersol.

[3] A mixture of *N*-myristyl-β-aminopropionic acid and *N*-lauryl-β-aminopropionic acid as their sodium salts, marketed by General Mills, Kankakee, Ill., under the trade name, Deriphat 170-C.

Table I—Apparent Rate Constants and Estimated Free Drug Fractions for Dialysis of Salicylate

Test Compd. and Concn.	k_1f, min.$^{-1}$ × 10^2	k_2, min.$^{-1}$ × 10^2	f
Control fluid	0.71	2.08	0.34
Control fluid	0.76	1.28	0.60
Control fluid	0.63	2.14	0.29
Control fluid	0.28	0.68	0.41
Control fluid	0.55	1.62	0.34
Control fluid	0.59	2.85	0.21
Control fluid	0.38	1.88	0.20
Control fluid	0.45	1.76	0.26
Control fluid	0.76	1.91	0.40
Control fluid	0.62	2.48	0.25
Average	0.57	1.87	0.33
DSS (dioctyl sodium sulfosuccinate), 0.02%	1.14	2.82	0.40
DSS, 0.2% plus stearyl dimethylamine, 0.2%	0.56	1.47	0.38
Sodium lauryl sulfate, 0.2%	1.91	5.00	0.38
Sodium lauryl sulfate, 0.2%	0.82	2.28	0.36
Sodium lauryl sulfate, 0.2%	0.60	2.83	0.21
Sodium lauryl sulfate, 0.2%	1.24	4.62	0.27
Sodium laurate, 0.1%	1.03	3.19	0.32
Sodium stearate, 0.15%	0.64	1.73	0.37
Stearyl trimethylammonium chloride, 0.1%	0.83	1.74	0.48
Cetyl trimethylammonium chloride, 0.02%	0.65	1.33	0.49
Lauryl trimethylammonium chloride, 0.02%	0.45	1.73	0.26
Lauryl trimethylammonium chloride, 0.05%	0.82	1.35	0.61
Lauryl trimethylammonium chloride, 0.1%	1.00	1.63	0.62[a]
Cetyl pyridinium chloride, 0.02%	1.29	2.58	0.50
Cetyl pyridinium chloride, 0.02%	1.26	3.89	0.32
Cetyl pyridinium chloride, 0.05%	1.40	2.07	0.68
Benzalkonium chloride, 0.02%	0.47	1.39	0.34
Tetraheptylammonium chloride, 0.25%	1.28	2.99	0.43
N-myristyl-β-aminopropionic acid, 0.25%[b]	1.42	3.18	0.45
N-myristyl-β-aminopropionic acid, 0.25%[b]	0.77	1.48	0.52
N-myristyl-β-aminopropionic acid, 0.5%	1.86	2.76	0.67
Dicoco dimethylammonium chloride, 0.02%	0.75	1.93	0.39
Polysorbate 80, 0.2%	0.59	0.95	0.62
Polysorbate 80, 2%	0.49	2.73	0.18
Polysorbate 80, 2%	1.22	3.92	0.31
2,2′-(Octadecylimino)diethanol, 0.5%	0.93	3.72	0.25
Stearyl dimethylamine, 0.2%	0.93	1.85	0.51[a]
Stearyl dimethylamine, 0.5%	0.90	1.77	0.51[a]
Dimethylaminoethanol, 0.2%	0.24	1.02	0.23
THAM [tris(hydroxymethyl)aminomethane], 1.8%	0.78	2.08	0.38
THAM, 1.8%	1.82	3.48	0.52
THAM, 1.8%	0.56	1.91	0.29
Dodecylammonium chloride, 0.025%	0.97	2.06	0.47[a]
Dodecylammonium chloride, 0.05%	1.22	2.14	0.57[a]
Dodecylammonium chloride, 0.1%	2.33	3.31	0.70[a]
Hexadecylamine, 0.05%	1.10	1.86	0.59
Octadecylamine, 0.05%	0.75	1.49	0.50
Octadecylamine, 0.1%	0.63	1.26	0.50
Octadecylamine, 0.1%	0.77	1.93	0.40
Heptylamine, 0.1%	0.34	1.57	0.21
Triethanolamine, 0.1%	0.57	3.26	0.18
Triethanolamine, 0.2%	0.68	2.64	0.26
Ethylenediamine, 1%	0.57	2.11	0.27
Hexadecylmorpholine, 0.25%	1.20	2.03	0.59
Ethylenediamine tetraacetic acid, 0.1%	0.28	1.03	0.27
Lecithin, 1%	0.25	1.50	0.17
p-Nitrophenol, 0.02%	0.45	1.87	0.24
Sodium taurocholate, 0.05%	0.56	2.55	0.22
Sodium deoxycholate, 0.01%	0.49	1.69	0.29
Atropine sulfate, 0.01%	0.44	1.86	0.24
Histamine phosphate, 0.01%	0.75		
PABA (*p*-aminobenzoic acid), 1%	0.82	1.47	0.56
PABA (*p*-aminobenzoic acid), 2.1%	0.94	1.90	0.49
PABA, 2.1% plus THAM, 1.2%	0.57	1.61	0.36
PABA, 2.1% plus lauryl trimethylammonium chloride, 0.5%	0.88	1.53	0.58
PABA, 2.1% plus DSS, 0.01%	1.19	2.75	0.43
PABA, 2.1% plus DSS, 0.02%	1.71	3.33	0.51
PABA, 2.1% plus sodium lauryl sulfate, 0.1%	1.51	3.53	0.43
PABA, 2.1% plus sodium lauryl sulfate, 0.1%	1.64	3.53	0.32
Anthranilic acid, 0.5%	0.65	1.36	0.48
Anthranilic acid, 0.5%	0.77	1.77	0.44
Anthranilic acid, 1%	1.51	3.17	0.47
Anthranilic acid, 1%	0.71	2.39	0.30
Anthranilic acid, 1%	0.93	2.69	0.34
Anthranilic acid, 1%	1.22	2.47	0.49
Anthranilic acid, 1%	1.50	3.17	0.47
Anthranilic acid, 2.1%	1.48	2.58	0.57
Anthranilic acid, 2.1%	1.01	1.85	0.55
Anthranilic acid, 2.1%	1.34	2.28	0.59
Anthranilic acid, 2.1%	1.73	2.72	0.64
Anthranilic acid, 2.1%	1.26	2.25	0.56
Anthranilic acid, 2.1% plus DSS, 0.01%	1.46	2.69	0.54
Anthranilic acid, 1% plus DSS, 0.02%	1.66	4.09	0.41
Anthranilic acid, 2.1% plus cetyl pyridinium chloride, 0.02%	2.06	2.97	0.69
Anthranilic acid, 2.1% plus cetyl pyridinium chloride, 0.02%	1.76	2.58	0.68
Anthranilic acid, 2.1% plus cetyl pyridinium chloride, 0.005%	2.10	3.47	0.61
Anthranilic acid, 2.1% plus *N*-myristyl-β-aminopropionic acid, 0.5%	2.15	2.71	0.79
Anthranilic acid, 2.1% plus *N*-myristyl-β-aminopropionic acid, 0.5%	1.83	2.69	0.69
Anthranilic acid, 0.5% plus *N*-myristyl-β-aminopropionic acid, 0.2%	1.27	2.38	0.53
Anthranilic acid, 0.2% plus *N*-myristyl-β-aminopropionic acid, 0.5%	1.27	1.87	0.68
Anthranilic acid, 0.1% plus *N*-myristyl-β-aminopropionic acid, 0.5%	1.38	2.16	0.64
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	2.58	3.90	0.65
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	2.20	3.19	0.69
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	1.84	2.90	0.63
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	2.48	3.62	0.69
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	2.05	3.03	0.68
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	2.24	3.61	0.74
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	2.30	4.00	0.58
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	1.91	3.80	0.50
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	1.94	3.41	0.57
M-1 fluid (anthranilic acid, 1% plus *N*-myristyl-β-aminopropionic acid, 0.25%	1.81	3.05	0.59
Average for M-1 fluid	2.14	3.45	0.63

[a] Animal died after sufficient data was obtained for calculation of constants. [b] A mixture of *N*-myristyl-β-aminopropionic acid and *N*-lauryl-β-amino-propionic acid as their sodium salts, marketed in 50% aqueous solution by General Mills, Kankakee, Ill., under the trade name, Deriphat 170-C. Percentages shown are of the aqueous solution as supplied.

appear likely that their effects on tissue binding might be different, therefore the combination of the two agents was studied in a number of animals. Results show that this combination gave a consistent increase in k_1f values averaging 3.7 times control and f values 1.9 times control.

Because of the encouraging results obtained with the combination of anthranilic acid 1% and *N*-myristyl-β-aminopropionic acid 0.25%, called M-1 fluid, this combination was selected for intermittent dialysis tests. Since the compounds might be expected to be absorbed rapidly from the peritoneum on the first exchange it was decided to use full-strength M-1 fluid in the first exchange and half-strength (M-1 fluid and control fluid, equal parts) in the second and subsequent exchanges. Three animals were run on this combination and three on control fluid, using the same procedure. Results are presented in Table II.

From Table II it is seen that M-1 fluid gave consistently high removal of salicylate, about three times as much as with control fluid. This ratio is not quite as high as the ratio of k_1f values obtained in the screening test, but this might be expected, since lowered blood level in one exchange reduces the amount removed in the next ex-

Table II—Intermittent Dialysis of Salicylate with M-1 and Control Fluids

Animal No.	Dwell Time, min.	Av. Plasma Level, mcg./ml.	Dialysate Concn., mcg./ml.	Amount Removed, % dose	Clearance, ml./min.	Cumulative Urinary Excretion, % dose
			Control Fluid			
R-123	35	342	29.9	1.55	0.33	7.6
	24	318	23.9	1.63	0.56	9.6
	24	287	20.2	1.05	0.40	12.7
	24	257	17.2	1.10	0.47	19.4
	24	248	17.4	1.04	0.46	22.6
			Total	6.37		
R-129	35	314	39.8	2.52	0.52	20.0
	24	295	24.2	1.63	0.54	20.7
	24	277	21.0	1.44	0.51	24.4
	24	265	17.6	1.27	0.47	30.6
	24	250	20.8	1.43	0.56	33.4
			Total	8.29		
R-131	35	315	34.1	1.60	0.36	19.0
	24	289	22.7	1.60	0.59	21.6
	24	268	19.2	1.08	0.43	26.4
	24	253	16.4	1.06	0.45	30.0
	24	238	15.8	1.02	0.46	36.3
			Total	6.36		
			M-1 Fluid			
R-128	35	251	90.7	4.35	1.24	15.6
	24	211	81.1	4.54	2.34	22.1
	24	180	68.3	5.12	3.08	23.0
	24	152	63.4	3.91	2.79	23.9
	24	129	55.2	3.88	3.25	24.4
			Total	21.80		
R-130	35	272	103.4	5.15	1.27	25.6
	24	233	73.3	4.40	1.93	26.9
	24	201	69.4	4.14	2.10	27.8
	24	172	57.5	3.33	1.98	28.6
	24	145	49.1	3.01	2.12	28.8
			Total	20.03		
R-132	35	266	91.9	5.37	1.56	27.9
	24	213	75.3	3.79	2.09	30.6
	24	182	70.0	4.82	3.11	31.2
	24	157	58.2	3.60	2.69	31.6
	24	139	50.7	2.93	2.47	32.0
			Total	20.51		

change even though the rate constant is the same. Also, the difference in clearances should be noted, M-1 fluid giving an average clearance of 4.8 times control. This comparison of clearances is somewhat misleading as will be discussed in the next section of this report.

DISCUSSION

The mechanism for transport of salicylate across the peritoneal membrane is not known. Previous work with pentobarbital (8) demonstrated that the membrane transport rate cannot be correlated with lipid/water partition coefficients with that drug, since the dissociated molecule passed the membrane at about the same rate as did the undissociated. Salicylate has been cited as having an affinity for certain components of the biological membrane and this may be the limiting factor in its transport (9). It may be speculated that the binding of salicylate to certain components of the membrane increases the stability of the closed configuration, thus restricting the passage of other salicylate molecules. It is also conceivable that the salicylate must dissociate from the first binding sites in the membrane and attach to other similar sites to progress through the membrane. In such case the degree of dissociation of the salicylate-site complex may be the factor limiting transport. This speculation led to the search for compounds of structure similar to salicylate which might displace it from binding sites in tissue. Whether the components of M-1 fluid displace salicylate from sites other than those on plasma proteins has yet to be determined, but this is worthy of further investigation.

It is noteworthy that with M-1 fluid the plasma levels of salicylate fell rapidly to levels below that expected from the amounts lost in dialysate and urine. This is explained by displacement of salicylate from serum protein, allowing a greater portion to pass through the capillaries into interstitial and intracellular water. By using estimates of plasma volume and other body fluids one can calculate the fraction of drug unbound in the plasma, assuming that in the other fluids to be unbound. These estimates indicate a rapid unbinding which increases with time and reaches values of free drug reasonably close to the f values obtained in the screening test.

Because the M-1 fluid drops the plasma level of salicylate as noted in the preceding paragraph, clearance values, which take into consideration the plasma level, are not suitable for comparison of rates of removal of salicylate by M-1 fluid and control.

Displacement of salicylate from plasma proteins calls attention to a precaution which must be observed in using such an agent in a case of poisoning. It is not known yet whether this type of agent will also displace the drug from binding at its site of toxic action. If it does not, displacement from plasma protein may be the equivalent of increasing the concentration in tissues and thus give a temporary increase in toxicity. If this is the case, it may be a proper procedure to use the displacing agent only after lowering the plasma level to a safe point. In a limited acute toxicity experiment on mice in this laboratory the M-1 fluid appeared to increase the toxicity of salicylate only slightly, but more detailed study will be given this problem in the future.

The M-1 fluid found in this work appears most promising as an accelerator for salicylate dialysis. The rate of removal is high enough that with continuous dialysis salicylate intoxication may be treated as effectively with this procedure as with the artificial kidney. Thus, this fluid may make possible a more effective treatment of salicylate poisoning by a means which can be utilized without the need for specialized personnel and equipment such as is required for hemodialysis.

It must be emphasized that the toxicity of M-1 fluid has not been studied sufficiently to justify its trial in man. It is hoped that this report will stimulate others to examine these materials to determine its safety for such use.

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