Effect of Complex Formation on Drug Absorption IX: Determination of the Intestinal Transfer Rate Constant of the Salicylamide-Caffeine Complex

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Abstract □ A model describing the overall transfer of a drug across biologic membranes in the presence of a complexing agent is presented. This model has been applied to the transfer of salicylamide across the cannulated everted intestine of the rat in the presence of caffeine. Assuming that (*a*) salicylamide and the salicylamide-caffeine complex are transferred at a rate proportional to their respective concentration gradient, and (*b*) the complex is not dissociated at the surface of the absorbing membrane, it is shown that $k_{app.}/k_{sam.} = k_{cmoplex}/k_{sam.} + F_f\ (1 - k_{complex}/k_{sam.})$, where $k_{app.}$, $k_{sam.}$, and $k_{complex}$ are intestinal transfer rate constants for salicylamide in the presence of caffeine, for salicylamide alone, and for the salicylamide-caffeine complex, respectively, and F_f is the fraction of total salicylamide which is not complexed. Since F_f is determined on the basis of an independently obtained stability constant (K_s) of the complex, an adequate fit of the intestinal transfer rate data to the model can be obtained only if the K_s at the transfer rate-limiting barrier of the intestine does not differ appreciably from that determined in the bulk solution. A plot of $k_{app.}/k_{sam.}$ *versus* F_f was linear, consistent with the model and the assumptions upon which it is based. The intestinal transfer rate constant of the salicylamide-caffeine complex was found to be considerably lower than that of salicylamide, but essentially the same as that of caffeine.

Keyphrases □ Complex formation—drug absorption □ Salicylamide-caffeine complex—transfer rate □ Everted intestine—test membrane, transfer rate □ Concentration gradient, salicylamide-caffeine—transfer rate effect □ Caffeine effect—salicylamide transfer □ Colorimetric analysis—spectrophotometer

Previous reports from this laboratory (1, 2) have dealt with certain physicochemical properties and intestinal transfer characteristics of the salicylamide-caffeine complexing system. Specifically, the extent of salicylamide complexation in a solution containing a high concentration of caffeine was measured directly (1), the apparent partition coefficient of the salicylamide-caffeine complex was determined experimentally and its significance with respect to intestinal absorption was analyzed theoretically, and an initial study of the transfer across the everted rat intestine of salicylamide, caffeine, and both drugs together was carried out (2). It was found that complexation of salicylamide with caffeine resulted in a decrease in the overall[1] intestinal transfer rate of salicylamide, but that it had no measurable effect on the overall intestinal transfer rate of caffeine (2). It was pointed out that factors which determine the rate of transfer of drug complexes across biologic membranes are likely to be identified only by focusing on the equilibria which exist at the surface of these membranes (2).

[1] In the context used in this paper, "overall" refers to the combined effect or behavior of free and complexed drug.

In this report a theoretical model is presented for the transfer of salicylamide across the everted rat intestine when part of this drug is complexed with caffeine. The applicability of the model has been tested by appropriately designed intestinal transfer studies. Several important implications of the fit of the experimental data to an equation derived from the model are discussed, and the intestinal transfer rate constant of the salicylamide-caffeine complex has been determined. The investigation described here exemplifies a general approach to the study of the effect of complex formation on drug absorption.

THEORETICAL

Assuming that free salicylamide and the salicylamide-caffeine complex are transferred across the cannulated everted rat intestine at a rate proportional to the respective concentration gradient of these species, the following relationship applies

$$k_{app.} = k_{sam.}\ (F_f) + k_{complex}\ (F_c) \qquad \text{(Eq. 1)}$$

where $k_{app.}$, $k_{sam.}$, and $k_{complex}$ are the intestinal transfer rate constants (3) of salicylamide in the presence of caffeine, salicylamide alone, and of the salicylamide-caffeine complex, respectively, and F_f and F_c are the fractions of total salicylamide in the drug solution which are free and complexed, respectively. If $(1 - F_f)$ is substituted for F_c in Eq. 1, the following equation is obtained after rearrangement:

$$k_{app.} = k_{complex} + F_f\ (k_{sam.} - k_{complex}) \qquad \text{(Eq. 2)}$$

If each side of Eq. 2 is divided by $k_{sam.}$, one obtains:

$$\frac{k_{app.}}{k_{sam.}} = \frac{k_{complex}}{k_{sam.}} + F_f \left[1 - \frac{k_{complex}}{k_{sam.}}\right] \qquad \text{(Eq. 3)}$$

If the assumptions on which the model is based are correct, a plot of $k_{app.}/k_{sam.}$ *versus* F_f should be linear, and the sum of the intercept and slope should be unity. Since F_f is ordinarily determined on the basis of the stability constant of the complex (K_s) obtained by independent physicochemical measurements, any pronounced difference in the value of K_s in bulk solution and in the microenvironment of the mucosal membrane,[2] respectively, would be reflected by a deviation of the data from linearity. While both Eq. 2 as well as Eq. 3 can be used to test the fit of the transfer-rate data to the model, Eq. 3 is likely to be more useful since the experimental variability between different intestinal preparations is reduced by determining both $k_{app.}$ and $k_{sam.}$ in the same intestinal segment. In order to determine the transfer-rate constant of the salicylamide-caffeine complex, $k_{complex}$, Eq. 2 can be rearranged to yield:

$$k_{complex} = \frac{k_{app.} - F_f\ k_{sam.}}{1 - F_f} \qquad \text{(Eq. 4)}$$

[2] If the microenvironment is in equilibrium with the bulk solution, the chemical potential of the various drug species would, of course, be the same in each phase. However, if the microenvironment represents a steady-state rather than an equilibrium situation, the possibility of a difference in K_s in the two phases becomes an important consideration.

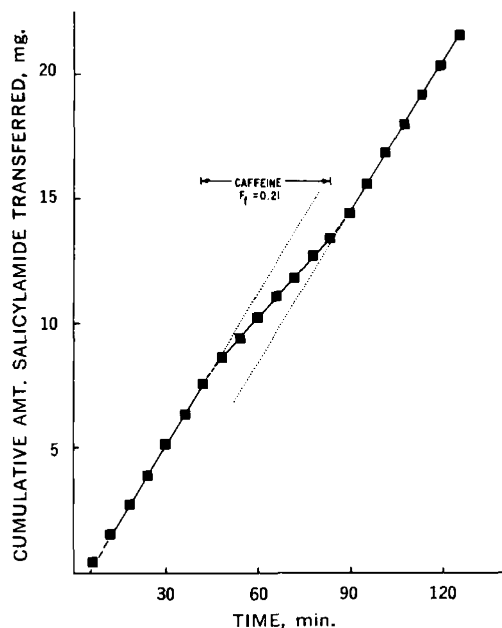

Figure 1—*Effect of a high concentration of caffeine (2.2%) on the transfer of salicylamide (0.384%) across an everted intestinal segment of the rat.* F_f, *the fraction of total salicylamide in the mucosal solution which is not complexed with caffeine, was not corrected or caffeine dimerization.*

where all the constants on the right-hand side are experimentally determinable.

EXPERIMENTAL

Intestinal Transfer Rate Measurements—The cannulated everted intestine method of Crane and Wilson (4) with modifications described in a preceding publication (2) was used to determine the intestinal transfer rate constants of salicylamide alone ($k_{sam.}$) and in the presence of caffeine ($k_{app.}$). A 10-cm. segment of everted intestine from the proximal ileum of rats weighing 210–380 g. was suspended in about 80 ml. of a solution containing the drug(s) dissolved in Krebs-Henseleit acetate Ringer solution (KHAR), pH 5.0 (mucosal solution). Oxygenation and agitation were accomplished by bubbling 5% CO_2 in O_2 through the mucosal solution. Two milliliters of Krebs-Henseleit bicarbonate Ringer solution (KHBR), pH 7.4, containing caffeine at a concentration equal to the calculated concentration of free caffeine in the mucosal solution, was introduced into the intestinal segment. This will be referred to as the serosal solution.[3] All the solution in the intestinal sac was removed every 6 min. The sac was then rinsed with 2 ml. of fresh serosal solution, which was combined with the previously withdrawn solution for subsequent assay, and another 2 ml. of fresh serosal solution was immediately placed into the sac. This frequent replacement of the serosal solution prevented significant buildup of salicylamide concentration on the serosal side (less than 15% of the mucosal salicylamide concentration). The serosal samples were then assayed colorimetrically for salicylamide, as described below. The transfer rates of salicylamide were determined from the slope of a plot of cumulative amount transferred *versus* time. Transfer rate constants were then calculated by dividing the transfer rate by the mucosal drug concentration. This was possible because the concentration of salicylamide in the mucosal solution remained essentially constant and was much higher than the salicylamide concentration in the serosal solution throughout the experiment (3).

Experimental Design—The intestinal transfer study was designed to determine the effect of complex formation on drug absorption under conditions where variability between different intestinal

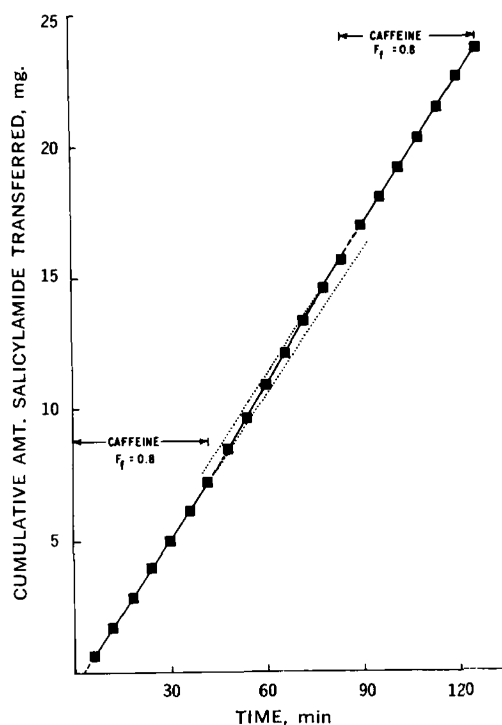

Figure 2—*Effect of a low concentration of caffeine (0.227%) on the transfer of salicylamide (0.384%) across an everted intestinal segment of the rat. The sequence of addition of caffeine was different rom that in the experiment depicted in Fig. 1.*

segments is minimized and where the extent of a possible alteration of membrane permeability during the experiment can be assessed. The everted intestinal segment was first suspended for 42 min. in a solution containing only the drug, then for 42 min. in a solution containing drug and complexing agent (CA), and then again for 42 min. in a solution containing only the drug. An equal number of experiments was carried out in the sequence drug-CA, drug alone, drug-CA. Comparison of the transfer rates observed in the first and third time periods permitted a determination of any possible

Table I—Values of $k_{app.}$ and $k_{sam.}$ Determined in Experiments with Everted Intestinal Segments of the Rat at Differing Values of F_f

Composition of Mucosal Solution,[a] % Salicylamide	Caffeine	Intestinal Transfer-Rate Constant, cm.³/hr. $k_{app.}$[b]	$k_{sam.}$[b]
0.384	2.200	1.99	3.36
		1.85	3.07
		2.09	3.18
		2.28	3.80
		Mean: 2.05	3.35
0.384	1.035	2.23	3.02
		2.49	3.36
		2.37	3.20
		2.64	3.74
		Mean: 2.43	3.33
0.384	0.532	2.63	3.31
		2.94	3.41
		2.67	3.30
		2.74	3.57
		Mean: 2.74	3.40
0.384	0.227	3.33	3.59
		3.56	3.91
		2.96	3.23
		3.41	3.56
		Mean: 3.32	3.57

[a] The solvent was KHAR, pH 5.0. [b] The determination of $k_{sam.}$ was made in the absence of caffeine. When caffeine was present in the mucosal solution for the measurement of $k_{app.}$, caffeine was also present in the serosal solution at a concentration equal to the calculated concentration of free caffeine in the mucosal solution. Each pair of $k_{app.}$ and $k_{sam.}$ values was determined in the same segment of intestine.

[3] No caffeine was added to the serosal solution when caffeine was not present in the mucosal solution.

changes in the permeability of the intestinal segment. The measurement of $k_{app.}$ and $k_{sam.}$ in the same segment of intestine markedly diminished the variability between results from different segments because division of $k_{app.}$ by $k_{sam.}$ in any one experiment cancels out any effects due to differences between segments in surface area, thickness of the gut wall, *etc*.

Intestinal transfer-rate measurements were made with mucosal solutions containing a constant concentration of total salicylamide (0.384%) and varying concentrations of caffeine (0%, 0.227%, 0.532%, 1.035%, and 2.2%). These solutions differed therefore with respect to F_f, the fraction of free salicylamide. Four experiments (two for each sequence described above) with different segments were carried out at each F_f and the four values of $k_{app.}/k_{sam.}$ for these segments were averaged.

Assay for Salicylamide—The samples of serosal solution were adjusted to pH 1 with 5 *N* HCl and subsequently diluted to 10 ml. with 0.1 *N* HCl. One milliliter of this diluted solution was added to 5 ml. Trinder reagent (5) contained in a 15-ml. centrifuge tube. The samples were shaken vigorously, centrifuged at about 3,300 × *g* for 20 min., and the absorbance of the clear solution was then determined at 525 mμ. Experiments in which known amounts of salicylamide and caffeine were added to the serosal solution obtained from a transfer experiment without drug (*i.e.*, only the solvents were used) showed that (*a*) caffeine does not interfere with the salicylamide assay; (*b*) the blank value of drug-free solvent which had been exposed for 6 min. to the intestine was negligible; and (*c*) the average recovery (six determinations) of salicylamide was 101% (*SD* 0.68%) in the range of concentrations encountered in the intestinal transfer study.

RESULTS AND DISCUSSION

The results of two representative experiments of the intestinal transfer study are presented in Figs. 1 and 2 and the results of all experiments are summarized in Table I. Figures 1 and 2 show the effect of the highest and lowest concentration of caffeine used in this study on the overall transfer rate of salicylamide. The linearity of the data in each time period, and the fact that the drug concentration buildup on the serosal side was practically negligible, permitted an accurate determination of the transfer rates and of the rate constants listed in Table I. It was found that the overall transfer rate of salicylamide decreases as the extent of complexation of this drug with caffeine is increased.

Fit of Intestinal Transfer-Rate Data to the Theoretical Model—The fit of the intestinal transfer-rate data to Eq. 3 (see *Theoretical*) is shown in Figs. 3 and 4. In Fig. 3, F_f was calculated by a method, outlined in a previous report (1), in which the dimerization of caffeine is neglected. In Fig. 4, F_f was corrected for caffeine dimerization. A direct experimental determination of the extent of complexation of salicylamide by caffeine has yielded results which are intermediate between those predicted by theoretical calculations in which dimerization has been neglected and corrected for, respectively (1). In either case, it is evident that the transfer-rate data are definitely consistent with the kinetic model proposed in the *Theoretical* section. The essentially linear nature of the relationship is evidenced by the very high correlation coefficient of 0.99 for the data in both Figs. 3 and 4.

An examination of Eq. 3 reveals that (*a*) when F_f = 1.0, $k_{app.}/k_{sam.}$ should be equal to unity, and (*b*) the sum of the slope and intercept of a plot of $k_{app.}/k_{sam.}$ *versus* F_f should be equal to unity. In Figs. 3 and 4, the 95% confidence intervals of the intercepts at F_f = 1.0 include the value of 1.0 for $k_{app.}/k_{sam.}$ Also, the sum of the slope and intercept of the line in each figure is very close to unity (Fig. 3, 1.03; Fig. 4, 1.05). These results support the assumptions on which the theoretical model is based, namely (*a*) the effect of caffeine on the overall intestinal transfer of salicylamide is due to complex formation; (*b*) the intestinal transfers of salicylamide and the salicylamide-caffeine complex are apparent first-order processes under the experimental conditions; and (*c*) the stability constant of the salicylamide-caffeine complex is the same in the microenvironment of the transfer rate-limiting biological barrier as in the bulk solution. Each of these assumptions will now be examined in detail.

Effect of Caffeine—The possibility that the effect of caffeine on the intestinal transfer of salicylamide may be due to a modification of membrane-permeability characteristics rather than to complex formation must be considered. The close agreement between the transfer rates of salicylamide in the first and third time periods (Figs. 1 and 2) indicates that there was no irreversible alteration in membrane permeability. Also, that the close agreement of the transfer-rate data with Eq. 3 makes a reversible alteration in intestinal permeability, occurring only when caffeine is actually present, seems quite unlikely. In a further test of the possibility of altered membrane permeability, transfer-rate experiments were carried out with two drug solutions containing differing concentrations of salicylamide and caffeine, but having the same value of F_f. This constitutes a direct test of the effect of caffeine concentration on the permeability characteristics of the intestinal barrier. The values of $k_{app.}/k_{sam.}$ obtained with these solutions (Table II) were not significantly different from each other ($p > 0.05$, *t* test). This indicates that there was no detectable reversible alteration in membrane permeability which was dependent on caffeine concentration. All of these results indicate that the effect of caffeine cannot be ascribed to either an irreversible or reversible alteration in membrane permeability. In addition, it was shown in a previous study (2) that intestinal metabolism of salicylamide is negligible under the experimental conditions and therefore does not contribute measurably to the intestinal transfer results. Thus, the effect of caffeine on the overall transfer of salicylamide is apparently due to complex formation.

Apparent First-Order Transfer—The fit of the intestinal transfer rate data to Eq. 3 strongly supports the assumption of apparent

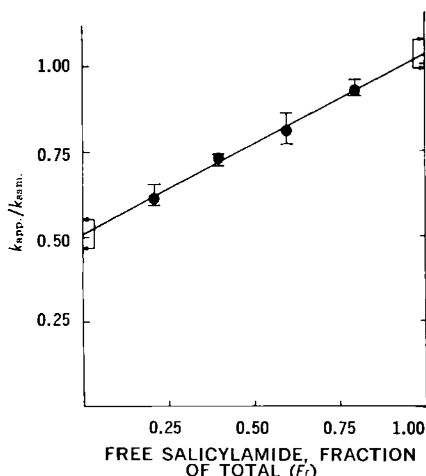

Figure 3—*Least-squares plot of* $k_{app.}/k_{sam.}$ *as a function of* F_f *not corrected for caffeine dimerization. Vertical bars indicate the range of the experimental values (4 experiments per data point) and arrows show the 95% confidence intervals of the two intercepts, as calculated from the 16 individual experiments.*

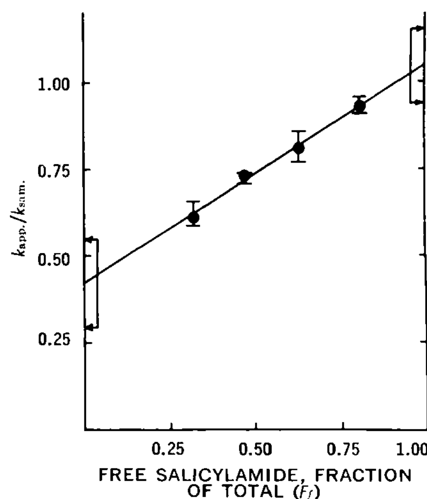

Figure 4—*Least-squares plot of* $k_{app.}/k_{sam.}$ *(average of four experiments each) as a function of* F_f *corrected for caffeine dimerization. Details as in Fig. 3.*

Table II—Determination of $k_{app.}$ and $k_{sam.}$ from Experiments with Different Concentrations of Salicylamide and Caffeine at Constant F_f

Composition of Mucosal Solution, %[a]	Fraction of Salicylamide Free (F_f)[b]	Intestinal Transfer-Rate Constant, cm.³/hr. $k_{app.}$	$k_{sam.}$	$k_{app.}/k_{sam.}$[c]
Salicylamide, 0.096	0.4	2.66	3.42	0.778
Caffeine, 0.790		2.78	3.66	0.760
		2.51	3.41	0.736
		2.81	3.54	0.794
		Mean: 2.69	3.51	0.767
Salicylamide, 0.384	0.4	2.23	3.02	0.738
Caffeine, 1.035		2.49	3.36	0.741
		2.37	3.20	0.741
		2.64	3.74	0.706
		Mean: 2.43	3.33	0.732

[a] The solvent was KHAR, pH 5.0. Caffeine was also present in the serosal solution at a concentration equal to the calculated concentration of free caffeine in the mucosal solution. [b] Calculated from the stability constant of the salicylamide-caffeine complex. [c] Both rate constants were determined in the same segment of intestine.

first-order transfer of both salicylamide and the salicylamide-caffeine complex. Further support for this assumption can be derived from the experiment described above in which the values of $k_{app.}$ and $k_{sam.}$ obtained at a high concentration of salicylamide and the salicylamide-caffeine complex were not significantly different from the values obtained at a lower concentration of these species.

The Stability Constant of the Salicylamide-Caffeine Complex in the Microenvironment of the Mucosal Membrane—The good fit of the intestinal transfer-rate data to the theoretical model suggests that the stability constant of the salicylamide-caffeine complex, which is used to calculate F_f, is the same at the site of transfer as that measured in the bulk solution (41.1 l./mole). However, to show this more definitively, it must be demonstrated that values of F_f calculated by assuming other values for the stability constant do not correlate linearly with $k_{app.}/k_{sam.}$. This test of the experimental data, the results of which are shown in Fig. 5, gives a definite indication of curvature at stability constants appreciably lower than that determined in the bulk solution. It is also evident from Fig. 5 that there is no pronounced curvature when the assumed stability constant is somewhat greater than that found in the bulk solution. However, the most likely effect at the membrane or in its immediate environment would be a decrease in the apparent stability constant of the drug complex rather than an increase. The definite curvature of the data calculated by assuming lower stability constants shows that the stability constant of the complex in the region adjacent to the transfer rate-limiting biological barrier is similar to that in the bulk solution.

The data in Fig. 5 rule out a dissociation of the drug complex prior to its transfer across the rate-limiting intestinal barrier. If the salicylamide-caffeine complex were not absorbed as such, the ratio $k_{app.}/k_{sam.}$ would be equal to F_f since only free salicylamide would be transferred. Using this value of F_f to calculate[4] a hypothetical stability constant of the complex (K_s) in the microenvironment of the mucosal membrane yields a value of 6.2 l./mole. A plot of $k_{app.}/k_{sam.}$ *versus* F_f based on F_f values calculated from a stability constant of 6.2 l./mole shows considerable curvature, which leads to the conclusion that the complex as such is transferred across the rate-limiting barrier of the intestine.

Determination of the Intestinal Transfer-Rate Constant of the Salicylamide-Caffeine Complex—With the validity of the proposed model established, Eq. 2 was used to calculate the intestinal transfer-rate constant of the salicylamide-caffeine complex itself ($k_{complex}$) from the experimental measurements of $k_{sam.}$ and $k_{app.}$. These constants are listed in Table III. The transfer-rate constant of the complex was considerably lower than that of salicylamide but was essentially equal to that of caffeine. This explains the fact that in the preceding study (2) the intestinal transfer rate of caffeine was not measurably affected by complex formation with salicylamide.

[4] The calculation may be carried out as follows: (*a*) $F_f = k_{app.}/k_{sam.}$, if only free salicylamide is absorbed in the presence of caffeine. (*b*) $S = F_f \cdot S_t$, where S is the molar concentration of free salicylamide and S_t is the total molar concentration of salicylamide. (*c*) $S\text{-}C = S_t - S$, where $S\text{-}C$ is the molar concentration of the salicylamide-caffeine complex. (*d*) $C = C_t - S\text{-}C$, where C is the molar concentration of free caffeine and C_t is the total molar concentration of caffeine. (*e*) $K_s = (1 - F_f)/F_f C$. This equation is a rearrangement of the following definition of F_f in which a substitution utilizing the definition of the stability constant, K_s, has been made: $F_f = 1/(1 + K_s C)$.

Table III—Intestinal Transfer-Rate Constant of the Salicylamide-Caffeine Complex[a]

	Transfer-Rate Constant, cm.³/hr.	95% Confidence Interval, cm.³/hr.
$k_{sam.}$	3.41[b]	3.27–3.55
$k_{complex}$, neglecting dimerization of caffeine	1.90[b]	1.72–2.08
$k_{complex}$, correcting for dimerization of caffeine	1.73[b]	1.52–1.94
$k_{caffeine}$	1.85[c]	1.61–2.09

[a] Calculated by means of Eq. 4. [b] Mean of the values from 16 segments. [c] Mean of the values from four segments, from *Reference 2.*

General Discussion—It is premature to attempt a definitive interpretation of the effect of complex formation on drug absorption on the basis of the physicochemical properties of the complex. It is already clear that conclusions or extrapolations based on apparent lipoid-aqueous partition coefficients obtained *in vitro* are unjustified and do not take account of the complexity of the *in vitro* and biological systems (2, 6). It will be necessary to study the absorption characteristics of a relatively large number of complexes with widely different physicochemical properties before meaningful generalizations can be attempted. Concurrent *in vitro* experiments with artificial lipoid membranes in series, and with artificial lipoid membranes covered by proteins or protein-like materials, may also be informative.

The use of adequate controls in studies of the effect of complex formation on drug absorption is essential. A distinction must be made between the *apparent* effects of complex formation on drug absorption (which may be mediated by changes in pH, solubility, dissolution rate, alterations of membrane permeability, or certain pharmacologic effects of the complexing agent), and a real effect due to the actual transfer of a drug complex across the biological barrier. The experimental and mathematical approaches outlined here and in preceding publications in this series permit (*a*) the direct determination of the extent of complex formation even in systems involving multiple simultaneous equilibria (1); (*b*) the estimation of the apparent stability constant of a drug complex at the absorption rate-limiting site of the biologic barrier; and (*c*) the determination of the absorption rate constant of the drug complex as such.

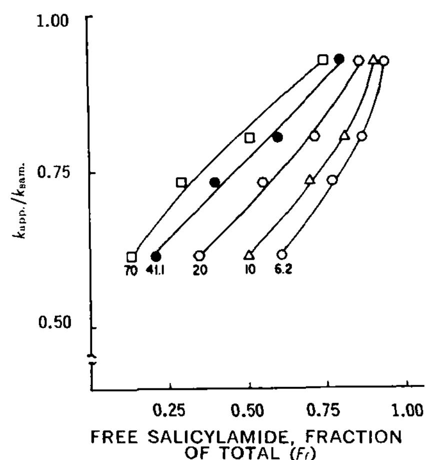

Figure 5—*Plot of* $k_{app.}/k_{sam.}$ *(average of four experiments each) as a function of* F_f*, assuming various stability constants of the salicylamide-caffeine complex, as shown in the figure. The* F_f *values were not corrected for caffeine dimerization.*

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ACKNOWLEDGMENTS AND ADDRESSES

Received May 27, 1968, from the *Biopharmaceutics Laboratory, Department of Pharmaceutics, School of Pharmacy, State University of New York at Buffalo, Buffalo, NY 14214*

Accepted for publication October 2, 1968.

Presented to the Basic Pharmaceutics Section, APhA Academy of Pharmaceutical Sciencies, Miami Beach meeting, May 1968.

This investigation was supported in part by grant R01-AM-08753-03 PET from the U. S. Public Health Service and by Public Health Service Predoctoral Fellowship No. F1-GM-24005 (for R.H.R.) from the National Institute of General Medical Sciences.

Previous paper: R. H. Reuning and G. Levy, *J. Pharm. Sci.*, **57**, 1342(1968).

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Water-Absorptive Properties of Selected Solids in a Lipophilic Base I

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Abstract □ Water-absorptive properties of various combinations of starch, pregelatinized maize starch, talc, and zinc oxide dispersed in light liquid petrolatum were investigated. The suction force and mercury rise were measured in terms of millibars with a tensiometer. The performance of these dispersions was evaluated in terms of two estimated parameters, $\hat{\alpha}$ and $\hat{\beta}$, which were related to absorption rate and absorptive capacity, respectively. Water-absorptive capacity varied in a predictable way while absorption rate did not. Zinc oxide had the highest absorptive capacity. Some interaction among the powders was noted by a decrease in suction force when various ones were mixed together.

Keyphrases □ Water absorption—solids in lipophilic bases □ Tensiometry—absorption analysis □ Powder interaction—absorption effect □ Absorption model—solids in lipophilic bases □ Diagram—tensiometer

The USP (1) describes pastes as preparations which are more absorptive than ointments due to a higher concentration of powdered medicaments. These pharmaceutical preparations often contain starch, talc, and zinc oxide in addition to other absorbants. They are used, in part, on the skin for absorbing water or exudation resulting from various skin diseases. One of the needs of the dermatologists is a paste which has a desiccant effect for treatment of exudatory dermatoses.

It would, therefore, be desirable to know which powder or combination of powders will be the most effective absorbant in a particular base. Rae (2, 3) reported on a method of testing absorption by various ointment bases as well as results for individually dispersed solids in a water-soluble base. This method was dependent upon the passage of water through a cellulose film and being absorbed by the particular powders.

Other methods used for measuring water absorption by ointments involved addition of water from a buret and mechanical treatment (4, 5), urea adduct method (6), and by drying loss, xylene distillation, and Karl Fischer titrimetric method (7).

The purpose of this research was to determine the absorptive powers of varying proportions of selected solids in a lipophilic base by utilizing a new method and procedure.

EXPERIMENTAL

Materials—The following materials were used for this experiment: starch, USP; pregelatinized maize starch[1]; talc, USP; zinc oxide, USP passed through No. 60 sieve; light liquid petrolatum, NF. The pregelatinized starch is a modified waxy maize starch which has instant swelling in cold water to produce clear dispersions. The moisture content of the dried starches never exceeded 5%.

Instrumentation and Methods—Tensiometers have been used since the 1920's to measure the absorbing power and suction force of soils (8–11). In its basic form, a tensiometer consists of a porous ceramic cup containing water in equilibrium with the water in the colloid (soil) surrounding, and in contact with, the cup. A mercury manometer connected to the cup measures the pressure (tension) with which the water in the cup is held. The experimentally measured quantity is the pressure difference, in millibars, across the porous wall of the cup.

Figures 1 and 2 show pictorial views of the instrument while Fig. 3 illustrates the essential parts of a tensiometer.[2] A porous ceramic cup, filled with air-free water, is attached to a connecting tube, which is in turn connected to a manometer or a vacuum gauge. Water in the surrounding medium is in hydrologic contact with the water inside the cup through the pores of the wall. As water is drawn through the cup wall, the depletion of water in the cup is reflected by changes in mercury level of the manometer.

Since the mercury manometer measures tensions (negative pressures) relative to atmospheric pressure, the maximum reading theoretically possible would be 1 atm. (1,013 mbar.). Very few tensiometers are reliable above 850 mbar., however. Other characteristics of tensiometers further limit their usefulness in measurements of water

[1] Instant Clearjel, National Starch and Chemical Corp., New York, N. Y.
[2] Tensiometer 6", cat. No. 2600 A, Soil Moisture Equipment Co., Santa Barbara, Calif.