Comparative Drug Adsorption by Activated Charcoal

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Abstract □ Comparative *in vitro* studies were carried out to determine the adsorption characteristics of 12 drugs on activated charcoal. At pH 1.3 and 37°, the adsorption capacity of activated charcoal (milligrams per gram of charcoal) was: aspirin, 262; glutethimide, 252; methaqualone, 179; chlordiazepoxide, 157; propoxyphene napsylate, 137; diazepam, 136; amitriptyline, 133; propoxyphene hydrochloride, 127; secobarbital, 124; pentobarbital, 103; phenobarbital, 70; and amobarbital, 51. The adsorption of the weak acids was most markedly decreased at pH 10.8. In patients, actual drug adsorption probably is lower than these maxima because of the presence of mucus, bile salts, and other drugs. In patients ingesting large amounts of poorly adsorbed drugs, activated charcoal would not be helpful.

Keyphrases □ Charcoal, activated—adsorption of various drugs *in vitro*, effect of pH □ Adsorption—various drugs to activated charcoal *in vitro*, effect of pH □ Analgesics—aspirin and propoxyphene, adsorption to activated charcoal *in vitro*, effect of pH □ Sedatives—glutethimide, methaqualone, diazepam, secobarbital, pentobarbital, phenobarbital, and amobarbital, adsorption to activated charcoal, effect of pH □ Tranquilizers—chlordiazepoxide, adsorption to activated charcoal *in vitro*, effect of pH □ Antidepressants—amitriptyline, adsorption to activated charcoal *in vitro*, effect of pH

Activated charcoal is frequently given to patients after acute drug ingestion (drug overdose) in an attempt to adsorb some ingested drug and thereby decrease the duration of the coma and/or the incidence of drug-induced morbidity. The efficacy of instilling activated charcoal down the lavage tube after lavage is not proven in adults (1).

The binding of psychoactive drugs to activated charcoal has been studied extensively. With rare exceptions, these studies are at nonphysiologic pH, in nonphysiologic solutions, at temperatures less than 37°, conducted in nonprimates, and seldom of a wide spectrum of chemical substances in the same study. Studies in humans are frequently anecdotal in nature and often pertain to children.

In *in vivo* animal studies, activated charcoal reduced GI absorption of phenobarbital (2), secobarbital (3), pentobarbital (2), glutethimide (3), propoxyphene (4–6), and aspirin (7, 8). Activated charcoal also significantly reduced GI absorption of drugs in humans (8–11).

As a prelude to efficacy studies of charcoal and other adsorbents in humans, the adsorption characteristics of various drugs on activated charcoal were determined.

EXPERIMENTAL

In vitro charcoal adsorption studies were carried out by dissolving psychoactive drugs in solutions at pH 1.3 and 10.8. Each liter of pH 1.3 solution contained: Na^+, 40 mEq; K^+, 10 mEq; and Cl^-, 95 mEq. Each liter of pH 10.8 solution contained: Na^+, 157 mEq; K^+, 10 mEq; Cl^-, 114 mEq; and HCO_3^{2-}, 106 mEq. Maximum adsorption wavelengths were determined[1] for each drug, and standard adsorption–concentration curves were prepared for each drug.

Twenty milliliters of solution containing 10–25 mg of drug was placed in a 50-ml centrifuge tube and incubated at 37° in a metabolic shaker. Various amounts of activated charcoal[2] (0.04–0.64 g) were then added to the tube carefully. The charcoal–drug solution was mixed, and incubation with shaking was continued for 15 min. The charcoal was allowed to settle for 5 min, and the supernate was then immediately filtered through a filter syringe[3]. The drug concentration in the simulated physiologic solution was determined spectrophotometrically after suitable dilution with 0.2 *M* carbonate buffer (pH 10).

RESULTS AND DISCUSSION

Experimental results on the adsorption of psychoactive drugs at pH 1.3 by activated charcoal are shown in Figs. 1 and 2. These data are plotted according to the Langmuir equation:

$$\frac{C_{eq}}{x/m} = \frac{C_{eq}}{k_2} + \frac{1}{k_1 k_2} \qquad \text{(Eq. 1)}$$

where C_{eq} is the free drug concentration in solution at equilibrium, x/m is the amount of drug adsorbed by the quantity of charcoal used, and k_2 and k_1k_2 are constants. The best straight line through these experimental data was calculated by the method of least squares, and the values of k_2 and k_1k_2 were evaluated from the reciprocals of the respective isotherm slope and intercept values of the regression equation.

Langmuir constants k_2 and k_1k_2 are summarized in Table I. The k_1k_2 values are relatively similar, presumably reflecting similar adsorption affinities between activated charcoal and the various drugs tested. However, since these values were calculated from the reciprocal of the intercept values of the Langmuir equation, k_1k_2 values are potentially subject to some error (12).

Aspirin was the most extensively bound (262 mg/g). A maximum binding capacity of 283 mg/g of charcoal at pH 1.0 was reported previously (11). Because large volumes of activated charcoal slurry may precipitate vomiting, one practice is to standardize the amount of charcoal by giving 1 g of activated charcoal/kg (13). Preferably, the dose of activated charcoal should be on the basis of the amount of drug ingested, but this information is seldom available. Therefore, the therapeutic need is to ensure that an excess of charcoal is given with minimal risk of vomiting. The present findings suggest that a dose of 1 g of activated charcoal/kg would adsorb 18.34 g of aspirin (*i.e.*, 58 300-mg tablets).

Whether propoxyphene is the napsylate or hydrochloride salt makes no difference to the adsorption of drug on charcoal. The benzodiazepines chlordiazepoxide and diazepam were adsorbed with intermediate capacity. Tablet equivalents of adsorption are: chlordiazepoxide, 400 25-mg tablets; and diazepam, 1904 5-mg tablets.

Figures 1 and 2 show the binding isotherms for the various drugs at pH 1.3, and Table I summarizes the results at both pH values. For sufficiently

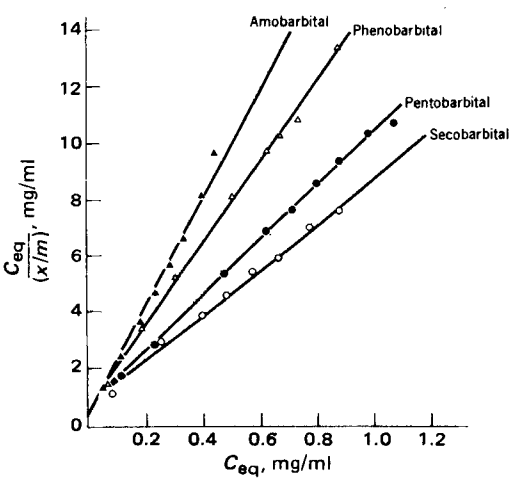

Figure 1—*Langmuir plots for barbiturate adsorption on activated charcoal at pH 1.3.*

[1] Beckman DBG UV spectrophotometer.
[2] Norit A, Fisher Scientific.
[3] Millipore Corp., Bedford, Mass.

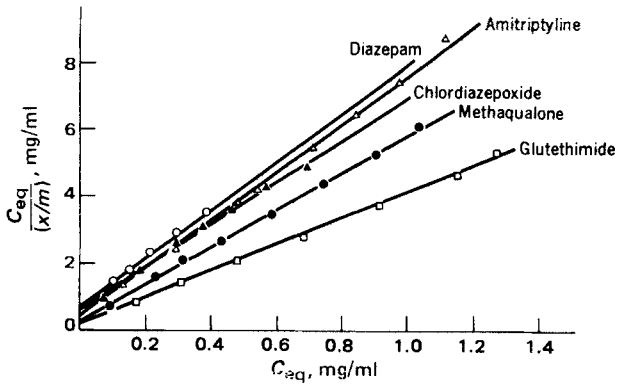

Figure 2—*Langmuir plots for adsorption of diazepam, amitriptyline, chlordiazepoxide, methaqualone, and glutethimide on activated charcoal at pH 1.3.*

soluble drugs, adsorption was less at the higher pH. The decrease in binding was greatest for aspirin (pKa 3.5). These results raise the possibility that aspirin adsorbed in the stomach may be transported adsorbed to charcoal into the small intestine where desorption occurs, with the consequent release of drug for absorption into the bloodstream.

Since patients may well ingest more drug than the charcoal's adsorption capacity, charcoal should not be used alone but be combined with emesis or lavage. Allowance should be made for giving larger amounts of charcoal to some patients, since the results of these *in vitro* studies probably represent maximum binding capacities. The capacities will likely be less in the presence of mucus, bile salts, blood, food, or alcohol, which more realistically represent the upper GI tract milieu in the overdose patient.

Table I—Values of Langmuir Constants Expressing Adsorption of Various Psychoactive Drugs by Activated Charcoal at pH 1.3 and 10.8, 37°

Drug	Charcoal Adsorbent (pH 1.3)		Charcoal Adsorbent (pH 10.8)	
	k_2[a]	k_1k_2	k_2[b]	k_1k_2
Amobarbital	51	3.44	47	1.20
Aspirin	262	3.08	141	1.23
Amitriptyline	133	3.72	—	—
Chlordiazepoxide	157	1.53	—	—
Diazepam	136	1.39	—	—
Methaqualone	179	3.51	—	—
Glutethimide	252	6.35	—	—
Pentobarbital	103	1.45	95	1.09
Phenobarbital	70	1.32	56	1.34
Propoxyphene hydrochloride	127	3.60	—	—
Propoxyphene napsylate	137	5.72	—	—
Secobarbital	124	1.53	85	2.19

[a] Milligrams of drug per gram of charcoal at 37°. [b] For seven drugs, solubility was insufficient to determine the adsorption isotherm accurately.

An additional complication is that frequently small amounts of a number of drugs are taken together, so competition for adsorption may occur. A dose of 100 g of activated charcoal would usually provide sufficient adsorption capacity. The current practice of lavaging patients before administering charcoal may not be optimal, and it might be possible to increase the efficiency of lavage by instilling the adsorbing substance *before* lavage as well as after.

Clinical studies in adults to determine the *in vivo* adsorption of drugs and the clinical efficacy of activated charcoal or other adsorbent materials such as ion-exchange resins are needed, since drug overdose seems to be increasing in incidence.

REFERENCES

(1) S. M. MacLeod, E. M. Sellers, H. Kaplan, and C. S. Stapleton, *Ann. Roy. Coll. Phys. Surg.*, **9**, 57 (1976).

(2) J. P. Atkinson and D. L. Azarnoff, *Clin. Toxicol.*, **4**, 31 (1971).

(3) W. J. Decker and D. G. Corby, *ibid.*, **3**, 1 (1970).

(4) D. G. Corby and W. J. Decker, *J. Am. Med. Assoc.*, **205**, 750 (1968).

(5) S. M. Chernish, R. L. Wolen, and B. E. Rodda, *Clin. Toxicol.*, **5**, 317 (1972).

(6) D. G. Corby and W. J. Decker, *J. Am. Med. Assoc.*, **203**, 1074 (1968).

(7) S. V. Phansalker and L. E. Holt, Jr., *J. Pediat.*, **72**, 683 (1968).

(8) W. J. Decker, D. G. Corby, and J. D. Ibanez, Jr., *Lancet*, **1**, 754 (1968).

(9) G. Levy and T. Tsuchiya, *Clin. Pharmacol. Ther.*, **13**, 317 (1972).

(10) W. J. Decker, R. A. Shpall, D. G. Corby, H. F. Combs, and C. E. Payne, *ibid.*, **10**, 710 (1969).

(11) T. Tsuchiya and G. Levy, *J. Pharm. Sci.*, **61**, 586 (1972).

(12) J. B. Milne and G. L. Chatten, *J. Pharm. Pharmacol.*, **9**, 686 (1959).

(13) R. E. Rangno, in, "Clinical Pharmacology of Psychoactive Drugs," E. M. Sellers, Ed., Alcoholism and Drug Addiction Research Foundation, Toronto, Canada, 1975, pp. 43–54.

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