(2.0–10.0 mg.). Prolonged contact with calcium-free Tyrode's solution produced a loss of spontaneous activity and a loss of effect of the extract. This was promptly reversed by the addition of $CaCl_2$ (4.0–10.0 mg.).

It seems likely, from the data, that the extract produces a direct musculotropic effect on strip motility and that this effect is mediated in some way through calcium. Analysis of the calcium content of strips after maximum response to the extract had occurred showed that the calcium content of extract-treated strips was decreased significantly when compared to that of control strips (Table I). This would seem to suggest that at least a part of the action of the extract involves an efflux of calcium from the strip. The question of whether this effect is related to other activities of the extract on the CNS and on skeletal muscle control is a subject for further study.

SUMMARY

This study involved testing an alkaloidal extract of *B. quitensis* on rabbit ileum in the presence of known stimulants and inhibitors of strip motility. Spontaneous contractions were inhibited, as well as those induced by methacholine, serotonin, $BaCl_2$, pilocarpine, nicotine, and $CaCl_2$. The inhibition was additive with inhibition produced by epinephrine, atropine, $MgCl_2$, or disodium ethylenediaminetetraacetate, and it was independent of α- and β-adrenergic receptors. A pharmacologic action involving efflux of calcium from the strips is postulated, based on the dependence upon adequate calcium for effect and the loss of calcium produced during response to the extract.

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Drug Adsorption Efficacy of Commercial Activated Charcoal Tablets *In Vitro* and in Man

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Abstract □ The *in vitro* adsorption characteristics and the inhibitory effect on drug absorption in man of commercial activated charcoal tablets and activated charcoal powder were determined, using phenylpropanolamine as the test drug. The rate and extent of drug adsorption on charcoal in tablets *in vitro* were much lower than on the charcoal powder. Under the conditions of the study, equal doses of charcoal tablets and powder reduced phenylpropanolamine absorption in healthy adult volunteers by 48 and 73%, respectively.

Keyphrases □ Charcoal tablets, activated, commercial—drug adsorption efficacy *in vitro*, in man □ Adsorption characteristics—commercial activated charcoal tablets, *in vitro*, in man □ Activated charcoal tablets—adsorption characteristics, *in vitro*, in man

Activated charcoal, administered as the pure powder dispersed in water, is an effective inhibitor of drug absorption and, therefore, a very useful antidote for many acute poisonings (1–3). The adsorptive capacity of activated charcoal is due mainly to its very large surface area and to the removal of previously adsorbed substances in the activation process. The question arises, therefore, whether or not activated charcoal tablets, which are available commercially, are effective clinically. In theory, the compaction of particles resulting from tablet compression and the addition of other constituents required for producing tablets should diminish appreciably the adsorption efficacy of activated charcoal. Comparative studies have been carried out with commercial tablets and activated charcoal powder, using phenylpropanolamine as the test drug.

EXPERIMENTAL

The activated charcoal tablets used contain 0.33 g. of the adsorbent per tablet and weigh about 0.44 g. each. Comparative studies were carried out with activated charcoal powder USP XVII[1]. Adsorption rates were determined *in vitro* by adding three tablets or 0.5 g. charcoal powder to 50-ml. portions of a 0.25% solution of phenylpropanolamine in 0.1 *N* HCl. These dispersions were agitated by a reciprocating shaker in a water bath at 37°, and three bottles of each were removed periodically for assay. The supernatant solution was filtered rapidly and the filtrate was analyzed for phenylpropanolamine by the method of Heimlich *et al.* (4). Equilibrium adsorption data for Langmuir adsorption isotherms were obtained by methods described previously (2). The disintegration time of the tablets was determined with the USP apparatus without disks in 0.1 *N* HCl at 37°.

Five healthy male volunteers, 22–31 years old, participated in the absorption study. Fifty milligrams of phenylpropanolamine was administered orally in 200 ml. water in the morning on an empty stomach. Charcoal was given immediately thereafter, dispersed in or (in case of the tablets) followed by a similar volume of water. Urine was collected at intervals until no additional drug excretion occurred (about 40 hr.) and was analyzed by the method of Heimlich *et al.* (4).

[1] Norit, American Norit Co., Inc., Jacksonville, Fla.

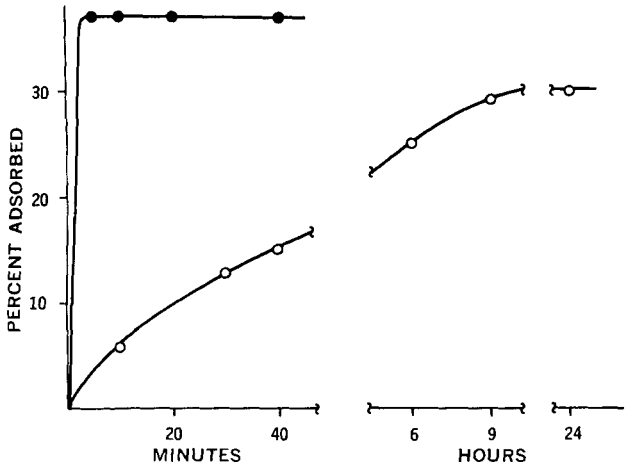

Figure 1—*Adsorption rate of phenylpropanolamine (125 mg. in 50 ml. 0.1 N HCl) on activated charcoal at 37°. Key: ●, 0.5 g. charcoal powder; and ○, 1.0 g. charcoal as three tablets. Each point represents the average result from three experiments.*

RESULTS AND DISCUSSION

Phenylpropanolamine was used as the test drug because: (*a*) activated charcoal is an effective inhibitor of the absorption of this drug in man, and (*b*) the amount of charcoal required for this purpose is relatively small (2). A preliminary study was carried out with aspirin as the test drug, but the large number of charcoal tablets required (more than 20 per dose) made a continuation of that investigation impractical.

The charcoal tablets had an average disintegration time of 83 min., with a large standard deviation (40 min. for six individually tested tablets). The *in vitro* adsorption rate of phenylpropanolamine on the charcoal powder was very rapid, but adsorption on the charcoal in tablets was very slow and equilibrium was attained only after 9 hr. (Fig. 1). Langmuir adsorption isotherms for the two forms of charcoal are shown in Fig. 2. The equation describing the isotherm for the tablets is $C/(x/m) = 5.5 + 22.7C$, where C is the concentration of phenylpropanolamine in milligrams per milliliter at equilibrium, and x/m is the amount of adsorbed drug in milligrams (x) per milligram of charcoal (m). The isotherm equation for the activated charcoal powder is $C/(x/m) = 0.6 + 10.1C$. The maximum adsorption capacity for phenylpropanolamine as calculated from these equations is 100 mg./g. adsorbent for the powder and 44 mg./g. for the tablets. Only the labeled content of activated charcoal—not the total tablet weight—was used in the calculations.

The absorption of phenylpropanolamine was determined from

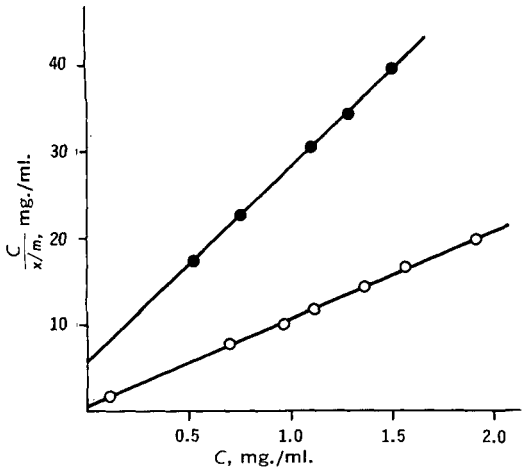

Figure 2—*Langmuir adsorption isotherms for adsorption of phenylpropanolamine on activated charcoal at pH 1, 37°. Key: ●, commercial tablets; and ○, powder. Each point represents the average result from three experiments.*

Table I—Effect of Activated Charcoal on Phenylpropanolamine Absorption in Man[a]

Subject	Percent of Dose Recovered in Urine—Charcoal, g. 0	2.0 as Tablets	2.0 Powder
T.T.	75.4	33.3	16.3
B.K.	79.4	39.3	23.1
W.H.	85.2	35.0	22.9
M.S.	80.1	60.5	17.5
P.G.	70.5	35.2	25.8
Mean	78.1	40.7	21.1
Relative availability	100	52.1	27.0
Statistical significance[b]		$p < 0.01$	$p < 0.05$

[a] Fifty milligrams phenylpropanolamine in 200 ml. water on an empty stomach. Charcoal was administered immediately after drug ingestion. [b] Paired t test.

urinary excretion data, using an aqueous solution of the drug without charcoal as the reference standard for the determination of relative bioavailability. Two grams of activated charcoal powder reduced phenylpropanolamine absorption by an average of 73%; the same amount of activated charcoal in tablets reduced drug absorption by only 48% (Table I).

The results of this study show that activated charcoal in tablets can be reasonably effective as an inhibitor of drug absorption in man. Since the source of activated charcoal in these tablets is not known, no estimate of the possible effect of the dosage form on the intrinsic adsorption efficacy of the charcoal can be made. The important point is that tableting does not necessarily reduce the efficacy of activated charcoal such that this adsorbent is no longer effective clinically.

The reasonably good efficacy of the tablets *in vivo* seems surprising in view of their very long disintegration times and the pronounced decrease in drug absorption rate relative to the charcoal powder. Under the experimental conditions, phenylpropanolamine absorption was reduced by 24 mg. by a dose of charcoal tablets with a theoretical maximum adsorption capacity of 88 mg. at low pH. This capacity can increase by about one-third as the pH increases to 8 (2). In the *in vitro* experiments, 24/88 or about 27% of equilibrium adsorption was attained within about 15 min. The corresponding adsorption rate *in vivo* is apparently sufficiently rapid to bind a significant fraction of the phenylpropanolamine dose before it is absorbed. This may not be true for drugs that are weak acids and are, therefore, absorbed more rapidly in most cases. A single absorption study with 1 g. aspirin (in solution) followed immediately by either 22 charcoal tablets or the equivalent amount of activated charcoal powder yielded data showing that aspirin absorption was reduced 38% by the powder and only 15% by the tablets. Thus, while activated charcoal tablets do have adsorptive activity in man, the use of activated charcoal *powder* is to be preferred for the initial treatment of acute poisoning.

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