Comparative Antidotal Effectiveness of Activated Charcoal, Arizona Montmorillonite, and Evaporated Milk

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Abstract □ Activated charcoal, Arizona montmorillonite, and evaporated milk were compared for their ability to reduce gastrointestinal absorption of three potential poisons. Time-course drug-concentration studies were performed on kerosene- and aspirin-treated animals. Activated charcoal and Arizona montmorillonite reduced blood kerosene level at all time periods studied, whereas evaporated milk was effective only during the early time periods. Activated charcoal reduced plasma aspirin level at all time periods studied, whereas Arizona montmorillonite was slightly effective only during the late time periods and evaporated milk was effective only during the initial few hours. Activated charcoal, Arizona montmorillonite, and evaporated milk reduced liver concentration of strychnine, which was analyzed only at the 5-min. time period, by approximately 80–90%. These antidotes also significantly elevated the median lethal dose (LD_{50}) of strychnine. Although activated charcoal appears to have the greatest adsorptive spectrum, Arizona montmorillonite and evaporated milk should be investigated further as possible antidotes.

Keyphrases □ Antidotal effectiveness—activated charcoal, Arizona montmorillonite, evaporated milk □ Aspirin, strychnine, kerosene poisoning—antidotes □ Arizona montmorillonite, activated charcoal, evaporated milk—comparative antidotal effectiveness

Activated charcoal has a wide spectrum of adsorptive activity (1–3) and is frequently recommended for the emergency management of ingested poisons (3–9). However, despite its effectiveness, there is some reluctance by the medical profession to use it because of its disagreeable appearance and because it stains clothing and linen (2). In the present investigation we evaluated two antidotes which have greater esthetic appeal than activated charcoal for their ability to inhibit gastrointestinal absorption of three potential poisons.

The first of these candidate antidotes is a clay mineral known as Arizona montmorillonite. It is prepared by elutriation of bentonite obtained from a clay deposit located in Northern Arizona and has the following formula (10):

$$(Al_{1.51}Fe_{0.13}Mg_{0.40})(Al_{0.07}Si_{3.93})O_{10}(OH)_2[Na_{0.02}(Ca_{0.37}/2)]$$

X-ray diffraction and fluorescence spectroscopy reveal that montmorillonite consists of hydrous aluminum silicate. It possesses a high specific surface area which has been determined to be approximately 780 $m.^2/g.$ The surface carries a high net negative charge and the chief cation on the surface is calcium. The cation exchange capacity has been calculated to be 148 meq./100 g. of clay. An aqueous suspension of finely powdered montmorillonite yields a preparation that is buff in color, is essentially odorless and tasteless, and has a slightly chalky texture.

The second candidate antidote is evaporated milk, a commodity which is readily available and is frequently found in homes. Evaporated milk is processed from fresh whole milk under partial vacuum at a temperature range of approximately 55 to 65° and adjusted to the legal requirement of 7.9% butterfat and 25.9% total milk solids (11, 12). The typical composition of evaporated milk is 73.7% water, 7% protein, 7.9% fat, 9.9% carbohydrate, and 1.5% ash (13). The finished product is then hermetically sealed in tins, subjected to heat sterilization (11, 12), and placed in shaking machines to break up the heat-coagulated casein (12).

Although milk is often recommended as an antidote for inhibiting gastrointestinal absorption of poisons (4, 5, 9, 14), there are few reports of experimental studies regarding its effectiveness as an adsorbent. One of these reports, published by Deaton *et al.* (15), concerns the use of milk to inhibit the gastrointestinal absorption of kerosene.

The primary aim of this investigation is to compare the relative effectiveness of activated charcoal, Arizona montmorillonite, and evaporated milk in their ability to inhibit gastrointestinal absorption of kerosene, aspirin, and strychnine. In addition, the time course studies which were performed serve to provide some information concerning the possibility of elution of two of the poisons from the various antidotes studied.

EXPERIMENTAL

Animals employed in this investigation consisted of male Sprague-Dawley rats weighing 225 to 275 g. and male mongrel dogs weighing 8 to 15 kg. All animals were fasted 24 hr. prior to drug administration but were allowed free access to water.

Kerosene, 8 ml./kg., was administered by oral intubation to four groups of 50 rats each. One minute later three of the groups were treated with activated charcoal[1] or Arizona montmorillonite, 3.6 g./kg., or evaporated milk,[2] each of which was administered orally in a volume of 20 ml./kg. Control rats received no additional treatment. Eight or nine rats from each group were anesthetized with ether at various time periods and blood was collected from the abdominal aorta and analyzed for kerosene according to the method of Guertin and Gerarde (16).

Aspirin, 100 mg./kg. in an aqueous suspension of 3 ml./kg., was administered by stomach tube to four groups of eight dogs each. One minute later three of the groups were treated with activated charcoal or Arizona montmorillonite, 500 mg./kg., or evaporated milk, each of which was administered orally in a volume of 10 ml./kg. Control dogs received no additional treatment. Serial blood samples were collected by venipuncture at various time periods and analyzed for aspirin by the method of Trinder (17).

Strychnine phosphate, 20 mg./kg. in a volume of 2 ml./kg., was administered by oral intubation to four groups of eight rats each. One minute later three of the groups were treated with activated charcoal or Arizona montmorillonite, 200 mg./kg., or evaporated milk, each of which was administered orally in a volume of 20 ml./kg. Control rats received no additional treatment. Five minutes after strychnine treatment each animal was anesthetized with ether and the liver was removed and analyzed for strychnine according

[1] Activated charcoal, Merck & Co., Inc., Rahway, N. J., was used throughout this investigation.

[2] Pet Evaporated Milk, Pet Inc., St. Louis, Mo., was used throughout this investigation.

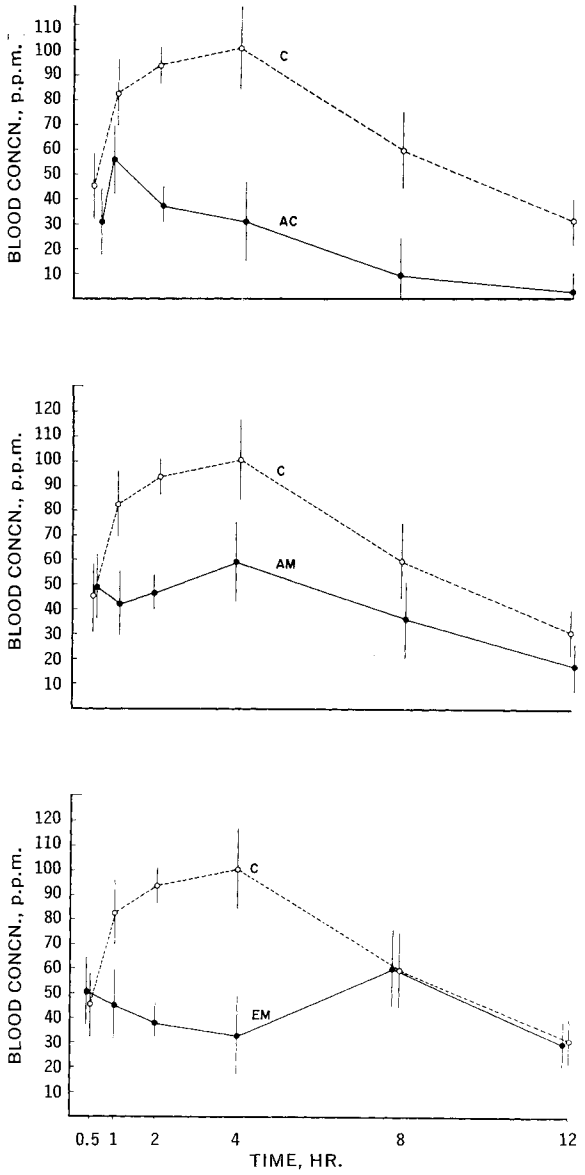

Figure 1—*The effect of activated charcoal, Arizona montmorillonite, and evaporated milk on blood concentration of kerosene in rats. All animals were administered kerosene, 8 ml./kg., by oral intubation. Each test animal was treated with one of the antidotes 1 min. later in a volume of 20 ml./kg. Key:* C, *control (kerosene only);* AC, *antidoted with activated charcoal, 3.6 g./kg.;* AM, *antidoted with Arizona montmorillonite, 3.6 g./kg.;* EM, *antidoted with evaporated milk, 20 ml./kg.*

to the method described by Picchioni *et al.* (6).

In addition, the relative ability of the candidate antidotes to elevate the median lethal dose (LD_{50}) of strychnine was compared. Strychnine phosphate, 5 to 40 mg./kg. in a constant volume of 2 ml./kg., was administered orally to groups of eight rats each. One minute after strychnine treatment various groups were treated with activated charcoal or Arizona montmorillonite, 200 mg./kg., or evaporated milk, each of which was administered orally in a volume of 20 ml./kg. During the LD_{50} determinations, each animal was individually maintained in a wire-mesh suspended cage and observed for death or survival. For each of the test and control studies, at least three dosage increments of strychnine which produced mortality between 0 and 100% were employed for the graphic calculation of the LD_{50}'s.

The results of the drug concentration studies were statistically evaluated by analysis of variance (18) and the results of the LD_{50} studies were analyzed according to the method of Litchfield and Wilcoxon (19).

RESULTS

The relative effectiveness of activated charcoal, Arizona montmorillonite, and evaporated milk in inhibiting the gastrointestinal absorption of kerosene is presented in Fig. 1. The mean blood kerosene level of rats treated with activated charcoal or Arizona montmorillonite is significantly lower than that of control rats at all time periods studied. The blood kerosene level in the evaporated milk-treated rats is significantly lower than that of control animals from the 1- to 4-hr. time periods. After the 4-hr. time period, the mean blood kerosene level of evaporated milk-treated animals increased so that by the 8-hr. time period the blood concentration curve of these test animals coincides with that of the control animals.

Figure 2 shows the mean plasma aspirin concentration of control and test dogs. Activated charcoal significantly decreased the mean plasma aspirin level at all time periods, especially during the early periods. Arizona montmorillonite failed to decrease plasma level of aspirin during the early time periods. However, at the 16- and 32-hr. time periods plasma aspirin level in Arizona montmorillonite-treated animals is slightly but significantly lower than in control animals. Evaporated milk significantly depressed mean plasma aspirin concentration only during the 0.5-, 1-, and 2-hr. time periods. From the 4-hr. time period on, the plasma aspirin curve of evaporated milk-treated animals is identical to that of the control animals.

Figure 3 shows the mean liver strychnine concentration of control and test rats 5 min. after the administration of the drug (4 min. after antidotal treatments). Activated charcoal and Arizona montmorillonite are equally effective in decreasing liver strychnine concentration, while evaporated milk is only slightly less effective.

Figure 4 shows the LD_{50} values of strychnine phosphate for control and test rats. Activated charcoal and Arizona montmorillonite are equally effective in elevating the LD_{50} of strychnine, while evaporated milk is only slightly less effective. In relationship to the liver strychnine concentration observations (Fig. 3), there appears to be good correlation between the ability of the various antidotes to elevate the LD_{50} of strychnine and their ability to reduce the liver concentration of strychnine.

DISCUSSION

The data presented substantiate the results of the previous investigations that activated charcoal is highly effective in reducing gastrointestinal absorption of various poisons (6, 20, 21). Also, as concluded in a previous investigation on a different series of chemicals (20), the flatter declining slopes of the blood kerosene and plasma aspirin curves of activated charcoal-treated animals as compared to the respective curves of control animals imply that adsorbed chemicals are released from charcoal in the gastrointestinal tract, but this effect appears to be of little practical consequence.

Arizona montmorillonite compares favorably with activated charcoal in its ability to reduce gastrointestinal absorption of kerosene and strychnine and in protecting rats against the lethal action of strychnine. The binding of chemicals by montmorillonite may involve adsorption and/or an ion-exchange reaction (22). The binding of kerosene by montmorillonite is likely due to an adsorption phenomenon because kerosene is a nonpolar chemical and ion-exchange would not be involved. Since Wai and Banker (22) have determined that brucine, the dimethoxy congener of strychnine, is bound by montmorillonite through adsorption and ion-exchange, it is likely that strychnine is bound by Arizona montmorillonite in a similar manner. In comparison to activated charcoal, Arizona montmorillonite has a poorer affinity for aspirin. The present observations on strychnine and aspirin concentration in Arizona montmorillonite-treated 6nimals and the previous investigation on Arizona montmorillonite (21) support the *in vitro* findings of Smith *et al.* (23) who reported that Alaskan montmorillonite is as effective as activated charcoal in binding certain cations but is inferior to activated charcoal in binding anions and organic acids. The blood kerosene curve of Arizona montmorillonite-treated rats which has a flatter declining slope than that of the control curve suggests that moderate elution of kerosene from Arizona montmorillonite occurs.

Evaporated milk is also effective in reducing or delaying the gastrointestinal absorption of various chemicals. However, according to the kerosene and aspirin time course studies, it does not appear to be as persistent in its action as activated charcoal. Release of chemicals from evaporated milk apparently occurs. The aspirin and

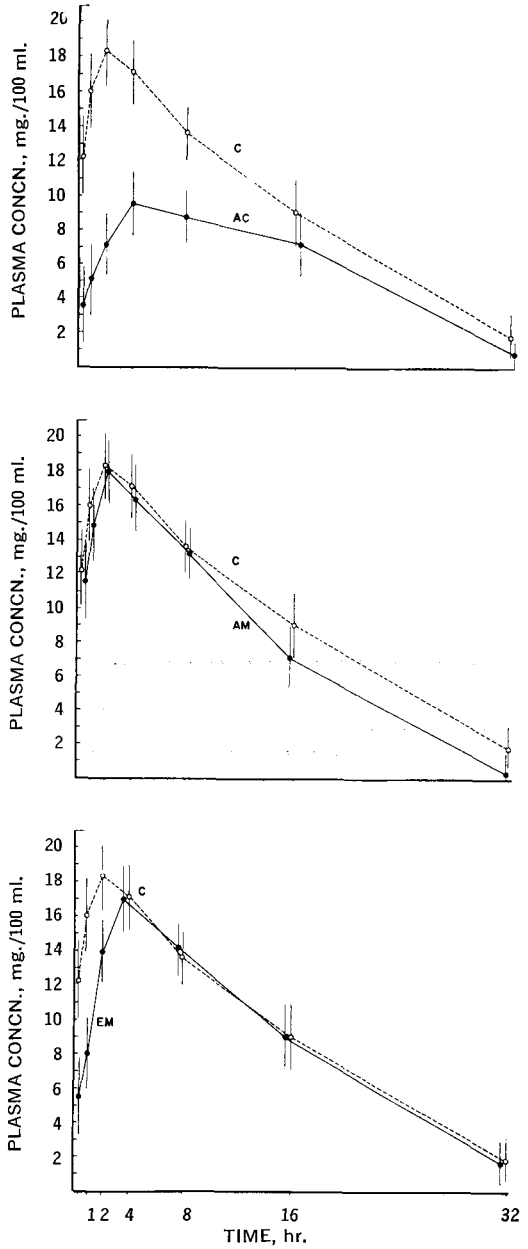

Figure 2—*The effect of activated charcoal, Arizona montmorillonite, and evaporated milk on plasma concentration of aspirin in dogs. All animals were administered aspirin, 100 mg./kg., by oral intubation. Each test animal was treated with one of the antidotes 1 min. later in a volume of 10 ml./kg. Key:* C, *control (aspirin only);* AC, *antidoted with activated charcoal, 500 mg./kg.;* AM, *antidoted with Arizona montmorillonite, 500 mg./kg.;* EM, *antidoted with evaporated milk, 10 ml./kg.*

kerosene curves of evaporated milk-treated animals are depressed during the early time period which suggest initial binding of the two chemicals by evaporated milk. The subsequent rise in the curves and the delayed peaking are suggestive of release of the chemicals from milk which resulted in increased gastrointestinal absorption of these chemicals. The mechanism by which evaporated milk reduces the gastrointestinal absorption of various chemicals is unknown. Milk has been presumed to work as an antidote through dilution (24), but Ferguson (25) and Henderson *et al.* (26) demonstrated that dilution with water tends to increase the rate and degree of gastrointestinal absorption of various chemicals. Hence, it is highly questionable that dilution contributes to the effectiveness of milk as an antidote. Bensley and Joron (4), on the other hand, suggest that the proteins of milk react with many poisons to form insoluble compounds. However, the warning has been advanced that this

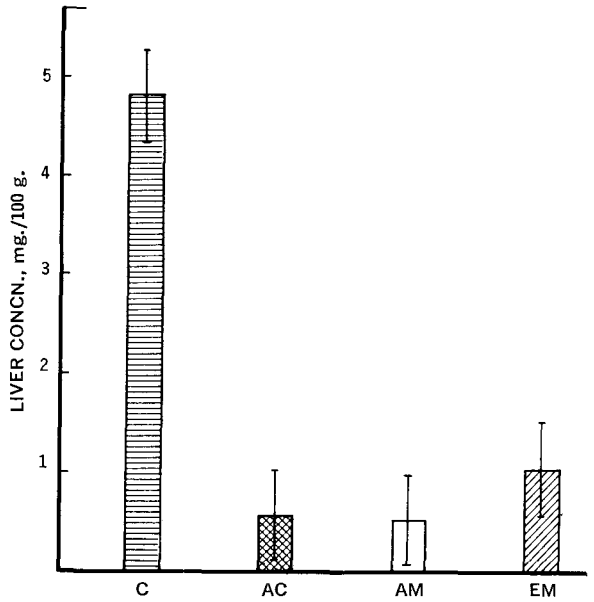

Figure 3—*The effect of activated charcoal, Arizona montmorillonite, and evaporated milk on liver concentration of strychnine in rats 5 min. after drug administration. All animals were administered strychnine phosphate, 20 mg./kg., by oral intubation. Each test animal was treated with one of the antidotes 1 min. later in a volume of 20 ml./kg. Key:* C, *control (strychnine phosphate only);* AC, *antidoted with activated charcoal, 200 mg./kg.;* AM, *antidoted with Arizona montmorillonite, 200 mg./kg.;* EM, *antidoted with evaporated milk, 20 ml./kg.*

detoxification effect of milk is temporary and that the milk-poison complex should be removed from the gastrointestinal tract (4, 27). The aspirin study in which evaporated milk is used as the antidote (see Fig. 2) supports the suggestion that gastric evacuation be performed when milk is used as an antidote. Another admonition concerning the use of milk as an antidote is that it must be avoided in the management of poisoning caused by fat-soluble chemicals

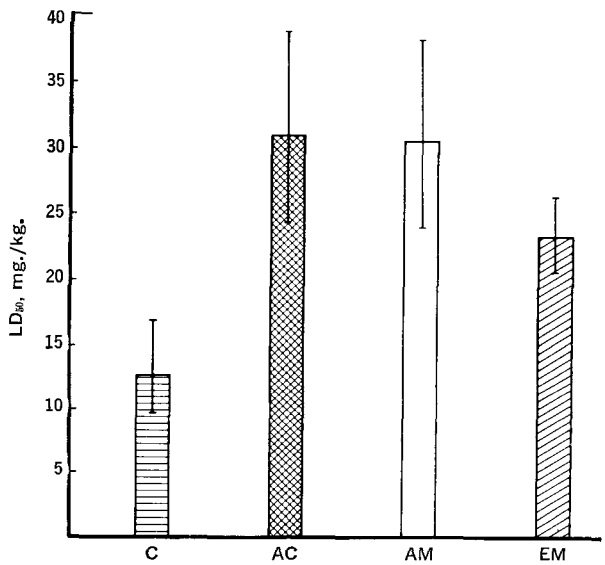

Figure 4—*The effect of activated charcoal, Arizona montmorillonite, and evaporated milk on median lethal dose (LD_{50}) of strychnine in rats. Groups of eight animals were administered strychnine phosphate in doses ranging from 5 to 40 mg./kg. by oral intubation. Each group of test animals was treated with one of the antidotes 1 min. later in a volume of 20 ml./kg. Key:* C, *control (strychnine phosphate only);* AC, *antidoted with activated charcoal, 200 mg./kg.;* AM, *antidoted with Arizona montmorillonite, 200 mg./kg.;* EM, *antidoted with evaporated milk, 20 ml./kg.*

because of the possible danger of enhanced gastrointestinal absorption of such poisons (4). However, the results of the kerosene study presented above (see Fig. 1) and the results reported by Deaton *et al.* (15) appear to contradict this view.

SUMMARY AND CONCLUSIONS

Of the three antidotes studied, activated charcoal undoubtedly has the broadest spectrum of adsorptive activity. Due to its poor affinity for anions and organic acids, Arizona montmorillonite lacks the breadth of antidotal activity of activated charcoal. But because it is highly effective in binding cations, has a surface area that compares favorably with that of activated charcoal, and possesses greater esthetic appeal than activated charcoal, additional investigations need to be performed on Arizona montmorillonite, especially with the aim of finding means to increase its spectrum of activity. Although evaporated milk appears to be less effective than activated charcoal as an antidote for ingested chemicals, its use to delay gastrointestinal absorption of poisons would be a practical first aid treatment since it does have a significant degree of effectiveness, is commonly found in the home, and would receive patient acceptance. Further studies of evaporated milk are in progress to determine its range of effectiveness and to determine further the stability or duration of its detoxification effect.

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