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Position Statement: Single-Dose Activated Charcoal

American Academy of Clinical Toxicology;
European Association of Poisons Centres
and Clinical Toxicologists

ABSTRACT

In preparing this Position Statement, all relevant scientific literature was identified and reviewed critically by acknowledged experts using agreed criteria. Well-conducted clinical and experimental studies were given precedence over anecdotal case reports and abstracts were not usually considered. A draft Position Statement was then produced and subjected to detailed peer review by an international group of clinical toxicologists chosen by the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists. The Position Statement went through multiple drafts before being approved by the boards of the two societies and being endorsed by other societies.

The Position Statement includes a summary statement for ease of use and is supported by detailed documentation which describes the scientific evidence on which the Statement is based.

Single-dose activated charcoal should not be administered routinely in the management of poisoned patients. Based on volunteer studies, the effectiveness of activated charcoal decreases with time; the greatest benefit is within 1 hour of ingestion. The administration of activated charcoal may be considered if a patient has ingested a potentially toxic amount of a poison (which is known to be adsorbed to charcoal) up to 1 hour previously; there are insufficient data to support or exclude its use after 1 hour of ingestion. There is no evidence that the administration of activated charcoal improves clinical outcome. Unless a patient has an intact or protected airway, the administration of charcoal is contraindicated.

The initial draft of this Position Statement was prepared by P A Chyka and D Seger.

This Position Statement is endorsed by the American Board of Applied Toxicology and the Canadian Association of Poison Control Centers.

SUMMARY STATEMENT

INTRODUCTION

- Overall, the mortality from acute poisoning is less than one percent. The challenge for clinicians managing poisoned patients is to identify promptly those who are most at risk of developing serious complications and who might potentially benefit, therefore, from gastrointestinal decontamination.

- Single-dose activated charcoal therapy involves the oral administration or instillation by nasogastric tube of an aqueous preparation of activated charcoal after the ingestion of a poison.

RATIONALE

- Activated charcoal comes in direct contact with and adsorbs poisons in the gastrointestinal tract, decreasing the extent of absorption of the poison, thereby reducing or preventing systemic toxicity.

IN VITRO STUDIES

- Scores of compounds, including many drugs, have been shown to be adsorbed to activated charcoal to varying degrees.[1]

ANIMAL STUDIES

- The administration of activated charcoal in animal studies has produced variable reduction in marker absorption.[1]

VOLUNTEER STUDIES

- The results of 115 comparisons with 43 drugs (Appendix 1) indicate considerable variation in the absolute amount of charcoal used (0.5–100 g) and the time of administration (up to 240 minutes after ingestion).

- In these studies, when activated charcoal was administered 30 minutes or less following drug administration (Table 1), the mean bioavailability was reduced by 69.1%. When activated charcoal was administered at 60 minutes following drug administration, the mean reduction in bioavailability was 34.4%.

- In 40 studies involving 26 drugs, using at least 50 g of activated charcoal, the mean reduction in drug absorption was 88.6% when charcoal was administered up to 30 minutes after dosing; mean reduction at 60 minutes was 37.3% (Table 2).

CLINICAL STUDIES

- There are no satisfactorily designed clinical studies assessing benefit from single-dose activated charcoal.

- One study[2] of symptomatic patients who received activated charcoal and some form of gastric evacuation (gastric lavage, ipecac, gastric aspiration) showed that patients receiving gastric aspiration and activated charcoal were less likely to be admitted to an intensive care unit.

INDICATIONS

- Based on volunteer studies, activated charcoal is more likely to produce benefit if administered within 1 hour of poison ingestion.

- The administration of activated charcoal may be considered if a patient has ingested a potentially toxic amount of a poison up to 1 hour following ingestion.

- Activated charcoal may be considered more than 1 hour after ingestion, but there are insufficient data to support or exclude its use.

DOSAGE REGIMEN

- The optimal dose of activated charcoal for poisoned patients is unknown, though available data imply a dose-response relationship that favors larger doses.

- Data derived from animal and human volunteer studies have little relevance to the clinical situation because these experimental studies were performed in fasting animals and human subjects who ingested a known quantity of drug.

- The *United States Pharmacopeia* (USP DI, 1997) recommends the following oral dosage regimen.
  Children up to one year of age: 1 g/kg
  Children 1 to 12 years of age: 25 to 50 g
  Adolescents and adults: 25 to 100 g

- Constipation has not been observed after the administration of a single dose of activated charcoal.

CONTRAINDICATIONS

- An unprotected airway.

- A gastrointestinal tract not anatomically intact.

- When activated charcoal therapy may increase the risk and severity of aspiration (e.g., hydrocarbons with a high aspiration potential).

COMPLICATIONS

Few serious adverse effects or complications from the use of single-dose activated charcoal have been reported in poisoned patients. Following the administration of aqueous activated charcoal, emesis occurs infrequently. However, the incidence of emesis appears to be greater when activated charcoal is administered with sorbitol.[25,59] With inadequate airway management, pulmonary aspiration has occurred following the administration of activated charcoal.[27] Aspiration of charcoal containing povidone has led occasionally to major respiratory problems.[7] Corneal abrasions may occur upon direct ocular contact.[60]

SUPPORTING DOCUMENTATION

INTRODUCTION

Single-dose activated charcoal has been used throughout this century for the treatment of poison ingestions.[1] The American Association of Poison Control Centers Toxic Exposure Surveillance System documented the use of single-dose activated charcoal in 142,805 of 2,155,952 (6.6%) exposures reported during 1996.[3]

Controlled pyrolysis of coconut shells, peat, lignite (coal), wood, or petroleum produces charcoal, which is then activated by heating it in steam, air, or carbon dioxide at 600–900°C. The charcoal is washed with inorganic acids and dried. Activation creates a highly developed internal pore structure and small particle size. These factors determine the extent of adsorption at equilibrium.[1] The adsorptive surface of activated charcoal contains several carbon moieties (e.g., carbonyl, hydroxyl) that adsorb a poison with varying affinity.[4] *In vitro* adsorption to activated charcoal in aqueous solutions is a nonspecific process that reaches equilibrium in less than 30 minutes.[5,6] Desorption of poison may occur because substance adsorption to activated charcoal is a reversible process[1] but the extent and clinical impact of this phenomenon have not been determined.

Medicinal charcoal must meet BP, USP, or similar standards for adsorption, microbial contaminants, and purity. It typically has a surface area of 950 to 2,000 m^2/g. A superactivated charcoal with a surface area of 3150 m^2/g is not currently available for therapeutic use and will not be considered in this Position Statement. Some aqueous formulations of activated charcoal contain preservatives, sorbitol, sodium bicarbonate, or povidone, which may cause complications[7] or potentially alter efficacy.[1,8–11] Tablets and capsules containing activated charcoal are unsuitable for the treatment of poisonings because the rate and extent of adsorption in *in vitro*[5,12] and human volunteer[5,13] studies are inferior to comparable amounts of powdered charcoal dispersed in water.

RATIONALE

Activated charcoal adsorbs the poison in the gastrointestinal tract, minimizing the extent of systemic absorption of the poison, thereby reducing or preventing systemic toxicity. In order for single-dose activated charcoal to be effective in reducing poison absorption, activated charcoal must come in direct contact with the poison. Furthermore, when indicated, activated charcoal should be used as soon as possible after ingestion of the poison, as delay in administration will reduce its effectiveness.

IN VITRO STUDIES

Methods to test the *in vitro* adsorption of substances to activated charcoal have been proposed

since 1900, but there is no international standard for medicinal charcoal. Different pharmacopeia (e.g., BP, USP) specify the use of different compounds, (e.g., phenol, antipyrine, iodine, methylene blue, or strychnine sulfate) to determine acceptable adsorptive properties of activated charcoal; these test compounds may not be representative of all important toxic compounds. Alternative techniques that are more representative of drug adsorption have been proposed.[9]

Adsorption to activated charcoal may be assessed *in vitro* either by calculating adsorption isotherms or by screening tests. Adsorption isotherms estimate the adsorptive capacity (i.e., the maximum amount of drug adsorbed by one gram of charcoal) for the substance at an equilibrium of adsorption and desorption by measuring the ratio of free to total drug over a range of charcoal to drug ratios. Both the total drug concentration and temperature are held constant. Screening tests involve a fixed concentration of a substance and activated charcoal in an aqueous system.

Using these experimental approaches, many compounds have been shown to be adsorbed to activated charcoal to some degree,[1,10,14] while others are adsorbed very poorly. The chief value of *in vitro* studies is to identify substances that are not adsorbed by activated charcoal.

In vitro experiments have demonstrated several factors that can influence adsorption to activated charcoal such as temperature, pore size of charcoal, particle size of charcoal, surface area of charcoal, solubility of the poison, ionization state of salts, pH, presence of inorganic salts, and gastric contents.[1,15,16] Although several of these factors may be considered in product formulation,[8] most of these factors cannot be controlled during the care of a poisoned patient. No consistent relationship between the maximum adsorptive capacity of activated charcoal and the physicochemical characteristics (e.g., pKa, molecular weight) of drugs has been elucidated to date.[17]

ANIMAL STUDIES

Several approaches have been used to demonstrate a diminution of pharmacologic or toxic effects, poison concentration, or systemic absorption in animals treated with activated charcoal.[1] Typically, these studies have used a control group receiving no activated charcoal. The application of these animal findings to humans involves problems with interspecies scaling such as differences in gastrointestinal motility and morphology, absorption rate and site, dose of poison and dosage form, and metabolism and elimination rates and pathways. Nevertheless, animal studies serve to confirm *in vitro* adsorption studies by demonstrating *in vivo* reduction in a poison's effect or absorption. Many animal studies reported statistical analysis of the data comparisons; others reported data compared with a control group deemed to be sufficiently different to interpret a change. Direct extrapolation of the findings in animal studies to human poisoning should be done cautiously, if at all.

VOLUNTEER STUDIES

Studies in human volunteers are based typically on comparative bioavailability studies of a test drug using a controlled, randomized, crossover design involving six to ten participants. Measures such as the area-under-the-curve (AUC) of drug concentration vs time or the extent of recovery of the drug in urine are employed depending on the properties of the drug. Since human volunteers are used as experimental subjects, only subtoxic doses of drugs have been studied.

Some studies have attempted to correlate *in vitro* adsorption to reduction in absorption.[18-21] Although these studies serve to confirm basic principles of adsorption, the results cannot be extrapolated directly to the care of a poisoned patient.

Extrapolation of data from human volunteer studies to patients who overdose is difficult because of the following factors: (1) variations in pharmacokinetics (e.g., differing dissolution, gastric emptying, and absorption rates) seen with toxic as opposed to therapeutic doses;[22] (2) variable delay in administration of activated charcoal; and (3) differences in the adsorptive properties of activated charcoal present in the stomach of a fasting human volunteer compared with the varying stomach contents of patients who overdose.

The results of 115 comparisons involving 43 drugs are tabulated in Appendix 1. There is considerable variation in the absolute amount of charcoal used (0.5–100 g) and the resulting gram-to-gram

ratio of charcoal to drug (1:1 to 100,000:1). The time delay for the administration of the charcoal was up to 240 minutes after drug administration.

Table 1 summarizes all data (115 comparisons) shown in Appendix 1. When activated charcoal was administered up to 30 minutes after dosing, the mean reduction in absorption was 69.1%; at 60 minutes the mean reduction was 34.4%. The data from 40 comparisons (26 drugs) using at least 50 g of activated charcoal are summarized in Table 2. The mean reduction in absorption was 88.6% when activated charcoal was administered up to 30 minutes after dosing; the mean reduction at 60 minutes was 37.3%. These volunteer studies demonstrate that irrespective of the dose of activated charcoal administered, the maximum reduction in drug absorption occurs when activated charcoal is administered within 30 minutes of drug dosing.

CLINICAL STUDIES

The 10 clinical studies purporting to evaluate the effectiveness of activated charcoal can be divided into three groups: six that had charcoal in both study arms;[2,23–27] three that had charcoal in one arm;[28–30] and two that compared charcoal to a no treatment control group.[2,31] These clinical studies have been criticized for their design[32,33] with many studies exhibiting shortcomings such as selection bias (weak randomization), no laboratory confirmation or correlation with history, insufficient number of severe cases, no control group, no quantitative measure of outcome, no stratification by severity in severe cases, no relation to time of ingestion for patient selection or data analysis, exclusion bias, and performance bias.

Activated Charcoal—Both Study Arms

Each of the following six studies compared activated charcoal to activated charcoal in combination with another therapy. Since activated charcoal was administered to both study groups, it is impossible to evaluate the effectiveness of activated charcoal. Nevertheless, these studies are reviewed here as they are often cited in support of the clinical use of activated charcoal.

Kulig *et al.*[23] reported a single institution, prospective study performed which included consecutive patients with an initial diagnosis of oral drug overdose. Exclusions included spontaneous or induced emesis, antecedent ipecac administration, the ingestion of hydrocarbons, corrosives, iron, strychnine, acetaminophen (paracetamol) alone, or ethanol alone. An alternate day allocation of treatments (activated charcoal and magnesium sulfate with gastric lavage or ipecac syrup vs activated charcoal 30–50 g with magnesium sulfate 20 g) was stratified by mental status of the patient upon arrival to the emergency department (ED). A total of 592 patients completed the study, of which 472 (79.7%) had a known time of ingestion and five (0.8%) were under 5 years of age. No difference was found between treatment groups based on clinical deterioration or improvement after initial ED assessment. In a subset of obtunded patients who received treatment within 1 hour of exposure, 16 out of 56 (28.6%) patients who were lavaged and given activated charcoal within 1 hour improved compared to 3 out of 32 (9.4%) ($p < 0.05$) who received only activated charcoal.

Albertson *et al.*[24] reported a single-institution, prospective study that included consecutive patients who presented to the ED with an oral drug overdose, were awake with an intact gag reflex, and were over 18 years of age. Patients were excluded if they had a rapidly deteriorating level of consciousness, spontaneous or induced emesis, antecedent ipecac or if the poison was a drug for which ipecac was contraindicated, an acid, a base, camphor, a volatile petroleum distillate, strychnine, iron alone, or lithium alone. Patients were assigned by hospital number to a treatment group of ipecac syrup 30 mL, followed by activated charcoal and sorbitol vs activated charcoal 1 g/kg with sorbitol. In the 200 patients completing the study, those receiving activated charcoal alone were discharged from the ED in significantly ($p < 0.05$) less time than those receiving ipecac and activated charcoal. For the hospitalized patients ($n = 25$), the duration of hospitalization, ICU admission rate, and duration of ICU stay were not statistically different between the two groups. A complication rate of 5.4% was found in the ipecac and activated charcoal group (aspiration occurred in four patients who had ingested a tricyclic antidepressant), whereas there was a complication rate of 0.9% in the activated charcoal group which was not related to the administration of activated charcoal.

Table 1

Summary of the Reduction of Drug Absorption by Single-Dose Activated Charcoal (0.5–100 g) in Human Volunteer Studies (n = 115). Comparisons Involving 43 Drugs at Varying Time Intervals (0–240 minutes) After Drug Dosing

% Reduction in Drug Absorption	Time (min) of Administration of Charcoal After Drug Dosing					
	0–5 (n = 81)*	30 (n = 9)	0–30 (n = 92)	60 (n = 17)	0–60 (n = 110)	> 60 (n = 5)
Mean	70.86	51.74	69.12	34.36	64.03	33.2
SD	± 29.37	± 17.97	± 28.85	±18.38	± 30.26	± 21.75
Median	85.0	49.4	77.15	29.7	64.65	37.5
Maximum	100.0	75.0	100.0	77.9	100.0	57.0
Minimum	10.0	28.8	10.0	5.7	5.7	8.4

*Number of studies

Table 2

Summary of the Reduction of Drug Absorption by Single-Dose Activated Charcoal (≥50 g) in Human Volunteer Studies (n = 40). Comparisons Involving 26 Drugs at Varying Time Intervals (0–60 minutes) After Drug Dosing

% Reduction in Drug Absorption	Time (min) of Administration of Charcoal After Drug Dosing				
	0–5 (n = 25)*	30 (n = 4)	0–30 (n = 29)	60 (n = 11)	0–60 (n = 40)
Mean	94.08	54.22	88.59	37.34	74.49
SD	9.10	17.32	17.29	18.21	28.93
Median	98.2	51.0	97.0	29.9	87.05
Maximum	100.0	75.0	100.0	77.9	100.0
Minimum	63.5	39.9	39.9	12.9	12.9

*Number of studies

Merigian *et al.*[2] reported a single-institution, prospective study involving consecutive adults with self-poisoning presenting to an ED. The interval between ingestion and treatment was unknown. Exclusion criteria included vomiting or the ingestion of the following substances: lithium, iron, heavy metals, monoamine oxidase inhibitors, digoxin, formaldehyde, mushrooms, acetaminophen (paracetmol), methanol, or sustained-release products. An alternate day allocation scheme for treatments was stratified by the presence of symptoms as assessed by clinical parameters at the time of presentation to the ED. Symptomatic patients (n = 357) were assigned to receive activated charcoal 50 g preceded by gastric lavage (n = 83) or activated charcoal 50 g preceded by ipecac vs nasogastric aspiration until stomach contents ceased to be returned followed by activated charcoal 50 g (n = 194). Patients who received activated charcoal and gastric aspiration were less likely ($p < 0.0001$) to be admitted to intensive care (n = 40, 20.6%) and more likely ($p < 0.0001$) to be admitted to a nonintensive care unit

(n = 72, 37.1%) compared to the group that received activated charcoal and gastric lavage or ipecac (n = 74, 45.4%; n = 20, 12.3%, respectively). The group that received gastric lavage or ipecac exhibited a four-fold greater rate of intubation ($p < 0.0001$) and ventilator use ($p < 0.0001$) compared to those who received only nasogastric aspiration and activated charcoal. Interpretation of this study is difficult as all three treatment groups received activated charcoal and some form of gastric evacuation. No group received activated charcoal alone.

Kornberg and Dolgin[25] conducted a single-institution, prospective study of consecutive patients who presented to the ED with an oral poisoning and were less than six years of age with a mild to moderate severity of poisoning. Exclusions included patients who were not alert or who had no definite gag reflex, those with a rapidly deteriorating level of consciousness, patients who exhibited spontaneous or induced emesis, those who had received antecedent ipecac, patients who had ingested a corrosive, hydrocarbon, iron, ethanol alone, or acetaminophen (paracetmol) alone, or patients who presented more than 6 hours after the time of ingestion. Patients were placed in treatment groups (ipecac syrup 15 mL followed by activated charcoal 1 g/kg with sorbitol vs activated charcoal 1 g/kg with sorbitol) on an alternate day allocation scheme. Seventy patients completed the study and three (4.3%) were subsequently admitted to the hospital. In an unreported number received confirmation of the history by a toxicological analysis screen. No differences in the outcomes were detected based on hospitalization rate and the proportion of patients who improved in the ED. Patients receiving ipecac syrup remained in the ED (4.1 ± 0.2 hour, SEM) for a longer period of time ($p < 0.05$) than those who received only activated charcoal (3.4 ± 0.2 hour).

Bosse *et al.*[26] conducted a prospective study of 51 patients who presented to a single institution following tricyclic antidepressant overdose and had a tricyclic antidepressant drug present in a urine drug screen. Patients were assigned every third day to one treatment regimen: activated charcoal 50 g and magnesium citrate 240 mL; gastric lavage followed by activated charcoal 50 g and magnesium citrate 240 mL; or activated charcoal 25 g followed by gastric lavage and activated charcoal 25 g with magnesium citrate 240 mL. No significant differences were demonstrated among the three treatments in the endpoints studied which included tricyclic-related symptoms, such as seizures, wide QRS or hypotension, and outcome measures, such as duration of hospitalization, duration of intensive care unit stay, or time on mechanical ventilation.

Pond *et al.*[27] reported a single-institution, prospective study that included consecutive patients who were 13 years of age and older with a history of ingestion of an overdose. Patient exclusion criteria included ingestions occurring more than 12 hours prior to arrival, treatment that breached the protocol, and if the ingested substance was not adsorbed to charcoal. Patients who vomited spontaneously were not excluded. Based on the patient's mental status at presentation to the ED, treatments (ipecac syrup or gastric lavage with activated charcoal and sorbitol (70%) 200 mL vs activated charcoal 50 g and sorbitol) were assigned by alternate day allocation. A total of 876 patients were included in the study which included 82 whose treatment did not adhere to the study protocol. No changes in the patients' condition or intubation rate were detected in the total or in the subset of patients treated within 6 hours of ingestion. Of the 30 patients treated within 1 hour of ingestion with activated charcoal and gastric evacuation, 13 of 21 (61.9%) patients demonstrated improvement ($p = 0.02$), whereas two of nine (22.2%) improved after activated charcoal alone. When the authors adjusted these data for severity, they reported no difference in the rate of deterioration ($p = 0.101$) or improvement ($p = 0.151$) between the treatment groups.

Activated Charcoal—One Study Arm

These three studies included only one study arm where activated charcoal was used. All three suffered from design flaws.

Comstock *et al.*[28] conducted a single-center, prospective study of a convenience sample of 339 adults who presented to the ED with acute drug overdose. All patients received gastric lavage and 131 patients were chosen in an unspecified random manner to receive activated charcoal 100 g after lavage. All patients had blood samples taken at the time of lavage and some had samples taken periodically for up to 21 hours thereafter. Of the

total population, 25 activated charcoal patients and 37 control patients had measurable blood concentrations of specified sedative-hypnotic drugs or aspirin and these patients constituted the initial population under study. This study population was reduced further because only 22 of 37 patients in the control group and 9 of 25 patients in the activated charcoal group had samples both in the 1- to 3-hour interval and in the 3- to 5-hour interval. There was no statistical difference between the lavage (control) group and the lavage plus charcoal group in the percentage of patients exhibiting increased blood drug concentrations. For the group of patients with moderate severity of symptoms, the mean residual blood drug concentrations declined significantly ($p < 0.05$) in the charcoal-treated patients at the 3- to 5-hour (four patients) and 5- to 9-hour (three patients) intervals compared with controls (12 and 9 patients, respectively). However, the experimental design of this study and statistical analysis of the data are seriously flawed and consequently these findings cannot be interpreted reliably.

Crome *et al.*[29] conducted a prospective study in an unspecified number of EDs which included adult patients with suspected antidepressant poisoning who were going to be admitted to the hospital. Patients were randomly allocated to one of two treatment groups: activated charcoal 10 g as Medicoal® (charcoal containing povidone and sodium bicarbonate) with supportive care or supportive care alone; an undetermined number of patients who also underwent gastric lavage. Although 48 patients entered the study, only 17 patients had taken tricyclic antidepressants alone according to laboratory analysis. The coma grades of these 17 patients were reported at intervals spanning 24 hours. There were an inadequate number of observations to make comparisons between the groups.

Hultén *et al.*[30] performed a four-center, prospective study for an unreported period of time that consisted of consecutive patients who presented to the ED after ingesting one or more of seven tricyclic antidepressant drugs and who were over 14 years of age. Allocation to a treatment group (gastric lavage vs gastric lavage plus activated charcoal 20 g as Medicoal) was performed by random numbers and adjusted by groups of 10. Drug concentrations and urine drug screens were determined in the patients and confirmed the history of the ingestion. A total of 77 patients (34 patients in the lavage/charcoal group and 43 patients in the lavage only group) completed the study. No statistical difference in the two treatments was detected based on the following: maximum serum drug concentration, half-life, presence of toxic symptoms, incidence of admission or duration of stay in the ICU, incidence or duration of intubation, need for ventilatory support, or duration of hospitalization. The lack of difference between the two groups might have been influenced by the small dose of activated charcoal used or the delay in administering activated charcoal after gastric lavage.

Activated Charcoal—No Treatment Control Group

At two hospitals, Underhill *et al.*[31] prospectively studied 60 patients who ingested at least 15 g of acetaminophen (paracetmol) within the previous 4 hours (mean 123 minutes, range 30–240 minutes). Patients were assigned randomly to one of the following three treatment groups at one hospital: gastric lavage, activated charcoal, or ipecac. At the other hospital, the study initially contained a fourth group receiving no treatment. However, the control arm of the study was stopped at five patients because serum acetaminophen concentrations increased between the first and last sample in four of these five patients. Blood samples for acetaminophen were taken prior to treatment, following treatment, and at 60, 90, and 150 minutes after the first sample. Although these data were presented graphically, there was no statistical analysis of charcoal-treated vs no-treatment groups.

Merigian *et al.*[2] investigated the outcome in 451 asymptomatic patients who received either activated charcoal 50 g or no treatment. Although there were no statistical differences in clinical outcomes between the two groups, there was no objective confirmation these patients had ingested a toxic dose of a substance, making interpretation problematic.

Case Reports

There are numerous cases in which activated charcoal has been used as one method of gastrointestinal decontamination. These case reports are difficult to assess, because they are uncontrolled, the histories are uncertain, and other therapies are often

used. Therefore, case reports have not been used to evaluate the effectiveness of activated charcoal, although they will be used to characterize the adverse effects associated with activated charcoal.

Impact of Activated Charcoal Dose

The optimal dose of activated charcoal for poisoned patients is unknown, although available data derived from experimental studies imply a dose-response relationship that favors larger doses.[18,19,34] Chin *et al.*[34] used a rat model to investigate the optimal antidotal dose of activated charcoal. The study (Table 3) quantifies the ability of activated charcoal to adsorb pentobarbital, chloroquine, and isoniazid with increasing charcoal to drug ratios of 1:1, 2:1, 4:1, and 8:1.

Table 3

Adsorption of Drugs to Charcoal at Different Charcoal to Drug Ratios in a Rat Model (After Chin et al.[34])

Drug	Charcoal: Drug Ratio	% Reduction ± SD) in Drug Concentrations
Phenobarbital	1:1	7.0 ± 2.6
	2:1	38 ± 3.5
	4:1	62 ± 3.7
	8:1	89 ± 2.2
Chloroquine	1:1	20 ± 8.2
	2:1	30 ± 6.5
	4:1	70 ± 1.5
	8:1	96 ± 1.4
Isoniazid	1:1	1.2 ± 1.2
	2:1	7.2 ± 2.6
	4:1	35 ± 5.3
	8:1	80 ± 1.6

The effect of charcoal-drug ratios on the antidotal efficacy of oral activated charcoal was studied in six human volunteers. Using a randomized crossover design, volunteers ingested sodium aminosalicylic (PAS) acid 1 g, 5 g, 10 g, or 20 g alone (control) and the same dose followed immediately by activated charcoal 50 g. Charcoal administered after PAS 1 g reduced bioavailability by over 95%, 5 g by almost 90%, 10 g by 75%, and 20 g by 63%. All values were statistically significant ($p < 0.05$) compared to control.[18]

Tsuchiya and Levy[19] studied five healthy male volunteers who were administered aspirin 1 g, salicylamide 1 g, or phenylpropanolamine 50 mg. Varying amounts (0.5 g–10 g) of activated charcoal were administered and the mean percent urinary recovery of each drug was compared to control. Mean salicylate recoveries in the urine were significantly ($p < 0.01$) reduced to 87.4% (charcoal 1.9 g) and 60.6% (charcoal 10 g). Urine salicylamide recovery following charcoal 1.5 g was 71.8% ($p < 0.01$) and 23.1% after charcoal 10 g ($p < 0.01$). The percentage of phenylpropanolamine recovered in the urine after charcoal 0.5 g was 42.0% ($p < 0.01$) and 5.2% ($p < 0.01$) after charcoal 5 g.

SPECIAL SITUATIONS

Boric Acid. Oderda *et al.*[35] conducted an *in vitro* study to determine the adsorptive capacity of activated charcoal 7.5 g, 15.0 g, and 30.0 g. The mean percentages adsorbed by a 1 g dose was 5.7 ± 1.6%, 17.6 ± 3.5%, and 38.6 ± 6.3%, respectively. The results after 15 g and 30 g were statistically less ($p < 0.05$) than after boric acid alone.

Cathartics. Since saline cathartics are occasionally coadministered with activated charcoal, several investigations have studied the potential interaction. There are conflicting data regarding the adsorptive capacity of activated charcoal for salicylates in the presence of magnesium citrate. Czajka and Konrad[36] found that magnesium citrate diminished the adsorptive capacity for aspirin by 14.9% ($p < 0.05$), whereas Ryan *et al.*[37] demonstrated that significantly ($p < 0.01$) more salicylate was adsorbed in the presence of magnesium citrate. Neither magnesium sulfate nor sodium sulfate demonstrated the same affinity as magnesium citrate.[36,37] The addition of sorbitol had no effect on the adsorption of acetaminophen (paracetmol),[38] but the adsorption of aminophylline was increased ($p < 0.05$) in the presence of sorbitol. (See the Position Statement on Cathartics for a more complete discussion.)

Cyanide. Andersen[39] demonstrated that charcoal 1 g could adsorb 35 mg of potassium cyanide *in vitro*. This has been interpreted as demonstrating a lack of adsorption compared to many other substances. However, as little as 200 mg of potassium cyanide is a potentially lethal dose in man, while 50 g of charcoal is a typical charcoal dose. This dose of charcoal could adsorb up to 1,750 mg of cyanide, equivalent to several lethal doses. The mortality rate in rats given potassium cyanide 35 mg/kg was reduced from 93% to 33% when a super-charcoal was administered immediately following exposure.[40] Moreover, mortality dropped from 100% to 27% when potassium cyanide 40 mg/kg was used. Relevance to other forms of cyanide or to the clinical situation when administration of charcoal is delayed is unknown, but it is quite likely to be relevant to other simple cyanide salts. In many cases, the rapid onset of life-threatening cyanide toxicity will obviate the usefulness of activated charcoal.

Ethanol. Ethanol is adsorbed by activated charcoal.[15,41] However, studies in dogs[42] and human volunteers[43] have not demonstrated a reduction in bioavailability. It is unclear whether the presence of ethanol decreases the effectiveness of activated charcoal to adsorb other toxic substances. Neuvonen *et al.*[44] demonstrated that the presence of ethanol reduced the *in vitro* adsorption of aspirin, quinidine, and amitriptyline presumably because ethanol altered solubility characteristics of these drugs. These same investigators[44] gave human volunteers charcoal 50 g 5 minutes after the ingestion of aspirin or quinidine. The coadministration of ethanol 50 g with the drugs had no significant impact on efficacy of activated charcoal. Olkkola[45] administered lethal doses of strychnine to mice and found a decrease in mortality when ethanol was also present in the gastrointestinal tract. These data do not contraindicate the use of activated charcoal in patients who have ingested ethanol and other drugs.

Hydrocarbons. Activated charcoal does adsorb several hydrocarbons.[1] When charcoal 3.6 g/kg was administered after oral instillation of hydrocarbon 8 mL/kg in rats, blood concentrations of kerosene were significantly reduced at all time points, (0.5, 1, 2, 4, 8, 12 hours).[46] Since the ingestion of many aliphatic hydrocarbons, such as gasoline and kerosene, is not likely to produce toxicity other than that associated with aspiration, the use of charcoal in these ingestions is typically not warranted and may cause or contribute to emesis and potential complications.

Ipecac. Activated charcoal adsorbs ipecac alkaloids.[47] Despite a report that coadministration of ipecac syrup 60 mL and activated charcoal 50 g did not abate the emetic effect in poisoned patients,[48] this approach is inconsistent with contemporary practice.

Lithium. Favin *et al.*[49] demonstrated no appreciable adsorption of lithium at acidic pH. Linakis *et al.*[50] gave lithium chloride 250 mg/kg and activated charcoal 6.7 g/kg to rats and found no difference in serum concentrations of lithium compared with control.

***N*-acetylcysteine.** Activated charcoal adsorbs *N*-acetylcysteine *in vitro*.[38,51-53] Adsorption isotherms were used to calculate activated charcoal adsorption of *N*-acetylcysteine at pH 7.5.[51] In simulated gastrointestinal fluid and nonbiologic fluid mediums, *N*-acetylcysteine (NAC) was adsorbed by activated charcoal, 746.9 $\pm$ 214.5 mg NAC/g charcoal and 4626.7 $\pm$ 386.6 mg NAC/g charcoal, respectively. There was a significant ($p < 0.01$) difference in adsorption to charcoal between the two fluids. Klein-Schwartz and Oderda[52] demonstrated that activated charcoal 3 g adsorbed 54.6 $\pm$ 9.4% and 3 g adsorbed 96.2 $\pm$ 4.3% of a NAC solution 200 mg/L ($p < 0.01$). Rybolt *et al.*[53] mixed *N*-acetylcysteine (3.26 mg/mL) with carbon powder 0.1, 0.2, 0.3, 0.4, and 0.5 g at pH 1.2 and 7.0. At pH 1.2 the percentages adsorbed were 9.3, 20.7, 27.1, 47.6, and 53.7%, respectively. At pH 7.0 the percentages adsorbed were 23.7, 45.6, 60.8, 72.6, and 77.2%, respectively. Van de Graff *et al.*[38] determined that *N*-acetylcysteine decreased the adsorptive capacity of two different activated charcoals by 12–18%.

Studies in human volunteers following administration of *N*-acetylcysteine 140 mg/kg demonstrated no decrease in bioavailability when charcoal doses of 50 or 60 g were employed.[54,55] However, the AUC was reduced by 39% ($p < 0.001$) after the administration of charcoal 100 g.[56] The serum concentrations in these studies were highly variable and difficult to interpret.[57]

INDICATIONS

Volunteer studies suggest that activated charcoal

is more likely to reduce poison absorption if it is administered within 1 hour of ingestion. In the absence of satisfactorily designed clinical studies demonstrating benefit from its use, the administration of activated charcoal may be considered if a patient has ingested a potentially toxic amount of a poison up to 1 hour following ingestion. There are insufficient data to support or exclude the use of activated charcoal when more than 1 hour has passed since ingestion.

DOSAGE REGIMEN

The wide range of the gram-to-gram ratios of charcoal to drug (1:1 to 100,000:1) in human volunteer studies (Appendix 1)—makes it difficult to infer the optimal dose of activated charcoal. Moreover, these experimental studies were performed on fasted subjects, who ingested a known quantity of drug, circumstances that are not commonly encountered in poisoned patients.

The *United States Pharmacopeia* (USP DI, 1997) recommends the following oral dosage regimen.

Children up to one year of age:	1 g/kg
Children 1 to 12 years of age:	25 to 50 g
Adolescents and adults:	25 to 100 g

CONTRAINDICATIONS

Activated charcoal is contraindicated if the patient has an unprotected airway, such as in a patient with a depressed state of consciousness without endotracheal intubation. Activated charcoal is also contraindicated if its use increases the risk and severity of aspiration (e.g., a hydrocarbon with a high aspiration potential). Patients who are at risk of hemorrhage, or gastrointestinal perforation due to pathology, recent surgery, or medical condition, could be further compromised by the administration of single-dose activated charcoal. The presence of activated charcoal in the gastrointestinal tract may obscure endoscopic visualization, but a corrosive is not a contraindication when charcoal is used for co-ingested agents that are systemic poisons.

COMPLICATIONS

Few adverse effects or complications from the use of single-dose activated charcoal have been reported despite its widespread use. In particular, there are no reports of gastrointestinal obstruction, constipation or hemorrhagic rectal ulceration associated with single-dose activated charcoal.

In four reports which used activated charcoal as a treatment arm, no complications were noted.[2,23,28,30] In patients receiving activated charcoal and sorbitol, Pond *et al.*[27] observed an overall complication rate of 3.6% (10/274) in alert patients and a rate of 18.8% in obtunded patients (25/133). However, there was no significant difference in the rate of complications observed in those who received gastric emptying (gastric lavage and activated charcoal with sorbitol or ipecac and activated charcoal with sorbitol) vs activated charcoal and sorbitol alone, irrespective of whether the patients were alert or obtunded and regardless of the time from ingestion to presentation. Pulmonary aspiration occurred in 1.7% (7/407) of patients who received only activated charcoal with sorbitol, but the contribution of activated charcoal alone was unclear.

There are few reports of emesis as a complication of charcoal administration. In a report of the prehospital use of charcoal without sorbitol, one of 14 patients vomited.[58] In a series of 20 patients who had ingested acetaminophen (paracetmol), three (15%) vomited after activated charcoal.[31] The addition of sorbitol increased the rate of emesis to 16%[25] and 56%[59] in two other studies. The influences of rate and volume of administration, ingested toxins, and premorbid conditions are unknown.

Two combative patients had charcoal spilled on their eyes during administration and developed transient corneal abrasions.[60]

In a clinical study of tricyclic antidepressant overdoses,[26] 2 of 22 patients (9.1%) aspirated. Five cases of pulmonary aspiration following single-dose activated charcoal have been described.[61-65]

An alert 8-month-old girl received ipecac syrup followed by activated charcoal 9 g in 35 mL of water via a nasogastric tube.[61] She vomited charcoal, became cyanotic, and cardiorespiratory resuscitation was initiated. Direct laryngoscopy revealed a trachea occluded with charcoal. After an eleven-day hospital course, she was sent home with normal chest radiographs and physical examination.

A 25-year-old male ingested alcohol and methaqualone.[62] He was obtunded in the ED where he received gastric lavage and activated charcoal via

an Ewald tube. He developed tension pneumothorax and a subsequent charcoal empyema probably as a consequence of gastric lavage-induced esophageal perforation. In addition, charcoal was observed in his sputum. After treatment with antibiotics he was discharged from the hospital without any symptoms.

A 16-year-old female ingested nortriptyline and was described as combative.[62] She was lavaged and charcoal 75 g was administered via nasogastric tube. Ten minutes later she had a grand mal seizure and a cardiac arrest. Following development of a right-sided pneumothorax, bronchoscopy revealed charcoal staining of both mainstem bronchi. She died many weeks later and at autopsy charcoal deposition was apparent throughout the airways and bronchiolitis obliterans was present.

A 30-year-old male had a depressed level of consciousness following an amitriptyline overdose.[64] Activated charcoal was instilled through the nasogastric tube which was in the right mainstem bronchus resulting in a decrease in oxygen saturation, wheezing, and subsequent ARDS. Bronchoscopic suctioning of the lungs returned copious amounts of charcoal. He was extubated after nine days.

Following an ingestion of tetracycline, a 20-year-old male received prehospital care that included placement of a nasogastric tube.[65] The patient vomited and pulled out the tube. The tube was replaced and activated charcoal was administered. Sorbitol was subsequently administered in the emergency department and the patient was released. The next day he returned in respiratory distress and required intubation. Endotracheal aspiration revealed charcoal-laden mucous. He recovered uneventfully.

Pulmonary aspiration associated with inadequate airway management and following lavage in an obtunded patient should not be considered a complication or an adverse effect of charcoal, since charcoal does not cause the aspiration. When aspiration does occur following the administration of charcoal, it is difficult to attribute subsequent pulmonary problems to the charcoal as opposed to the gastric contents. Aqueous activated charcoal in the gastric aspirate probably does not increase the complication rate of aspiration, although the inclusion of povidone increases pulmonary complications.[7] Fungal contamination of activated charcoal[66] may complicate pulmonary aspiration, but this problem of contamination is rare and isolated. The complications following aspiration of activated charcoal *per se* are consistent with those following the aspiration of gastric contents.

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Appendix 1 appears on the following pages.

Appendix 1

Randomized Controlled Trials of Single-Dose Activated Charcoal in Human Volunteers

Drug	Dose	n	Activated Charcoal Dose (g)	Activated Charcoal Form[a]	Activated Charcoal Delay[b] (min)	Bioavailability (Mean ± SD)[c,d] Control	Bioavailability (Mean ± SD)[c,d] Charcoal	Percent Reduction[e]	Ref
Acetaminophen	1000 mg	8	10	1	0	89.6 ± 10.7	56.5 ± 24.3‡	36.9[A]	67
Acetaminophen	1000 mg	5	5	1	0	83.0	43.8‡	47.2[A]	68
Acetaminophen	1000 mg	5	10	1	0	83.0	32.0‡	61.4[A]	68
Acetaminophen	1000 mg	5	10	1	30	83.0	57.2†	31.1[A]	68
Acetaminophen	3000 mg	10	50	1,4	60	119.41	88.92*	25.5	69
Acetaminophen	1000 mg	6	50	2	5	100.0	15.0†	85.0[B]	70
Acetaminophen	1000 mg	6	50	2	30	100.0	60.0*	40.0[B]	70
Aminophylline	350 mg SR	6	50	2	5	100.0	19.0†	81.0[B]	70
Aminophylline	350 mg SR	6	50	2	30	100.0	25.0*	75.0[B]	70
Amiodarone	400 mg	6	25	2	0	6.82 ± 0.82[H]	0.16 ± 0.05‡	97.7	71
Amiodarone	400 mg	6	25	2	90	6.82 ± 0.82[H]	3.40 ± 1.0*	50.1[I]	71
Amitriptyline	75 mg	6	50	2	0	3.91 ± 0.51[E,H]	unmeasurable‡	100.0	72
Ampicillin	5000 mg	10	50	3,5	60	50.2 ± 10.7[H]	21.8 ± 2.4†	56.6	73
Atenolol	100 mg	7	25	2	5	9.05 ± 0.67[H]	0.81 ± 0.10*	91.0	74
Carbamazepine	400 mg	5	50	2	< 5	258 ± 15[H]	< 10.0*	100.0	75
Carbamazepine	400 mg	5	50	2	60	258 ± 15[H]	153 ± 33*	40.7	75
Carbamazepine	400 mg	6	8	2	< 5	165 ± 3.7[H]	11 ± 4.7*	93.3	76
Chloroquine	500 mg	6	25	2	< 5	7.27 ± 0.825[E,H]	0.062 ± 0.046†	99.1	77
Chlorpropamide	250 mg	6	50	2	5	2581 ± 207[H]	12.7 ± 3.8‡	99.5	78
Cimetidine	400 mg	7	50	2	5	8.25 ± 0.85[H]	unmeasurable†	100.0	79
Ciprofloxacin	500 mg	6	1	4	< 5	13.36 ± 3.98	12.02 ± 3.19	10.0	80
Digoxin	0.25 mg	6	8	2	< 5	14.3 ± 1.3[D,H]	0.2 ± 0.1*	98.6	76
Digoxin	0.50 mg	6	50	2	< 5	36.4 ± 4.3[D,H]	2.8 ± 11†	92.3	81
Digoxin	0.50 mg	6	50	2	60	36.4 ± 4.3[D,H]	25.6 ± 2.2*	29.7	81
Diphenhydramine	50 mg	6	50	2	5	757 ± 366[D]	unmeasurable*	100.0	20
Diphenhydramine	50 mg	6	50	2	60	757 ± 366[D]	575 ± 273	24.0	20

Disopyramide	200 mg	6	2.5	2	< 5	38.8 ± 7.8[H]	15.9 ± 3.5*	59.0	82
Disopyramide	200 mg	6	10	2	< 5	38.8 ± 7.8[H]	4.2 ± 1.9*	89.2	82
Disopyramide	200 mg	6	25	2	< 5	38.8 ± 7.8[H]	1.4 ± 0.6*	96.4	82
Disopyramide	200 mg	6	50	2	< 5	38.8 ± 7.8[H]	1.4 ± 0.6*	96.4	82
Disopyramide	200 mg	6	2.5	2	< 5	30.1 ± 2.2[H]	6.8 ± 1.8*	77.4	82
Furosemide	40 mg	6	8	2	< 5	3.5 ± 0.75[H]	0.03 ± 0.02*	99.1	76
Glipizide	10 mg	6	8	2	0	1830 ± 267[D,H]	352 ± 128†	80.8	83
Indomethacin	50 mg	6	2.5	2	< 5	8.9 ± 1.5[H]	3.1 ± 0.6*	65.2	82
Indomethacin	50 mg	6	10	2	< 5	8.9 ± 1.5[H]	1.3 ± 0.3*	85.4	82
Indomethacin	50 mg	6	25	2	< 5	8.9 ± 1.5[H]	0.8 ± 0.2*	91.0	82
Indomethacin	50 mg	6	50	2	< 5	8.9 ± 1.5[H]	0.5 ± 0.2*	94.4	82
Isoniazid	600 mg	4	10	6	0	46.3	34.3	25.9	84
Isoniazid	10 mg/kg	3	60	1	0	100.0	unmeasurable*	100.0[B]	85
Mefenamic acid	500 mg	9	2.5	6	60	1.843 ± 715	1.180 ± 551‡	36.0	86
Mexiletine	200 mg	6	25	2	< 5	2.82 ± 0.37[H]	0.10 ± 0.05	96.5	87
Mexiletine	200 mg	6	25	2	60	2.82 ± 0.37[H]	2.66 ± 0.33	5.7	87
N-acetylcysteine	140 mg/kg	21	100	1	30	5,799 ± 1,756[G]	3,484 ± 1,398‡	39.9	56
N-acetylcysteine	140 mg/kg	6	60	1	0	3,019 ± 1,244	2,466 ± 936	18.3	55
Nizatidine	150 mg	11	2	1	60	3120 ± 372[D]	2,410 ± 591*	22.8	88
Nortriptyline	1 mg/kg	6	5	4	30	100.0	71.2*	28.8[B]	89
Nortriptyline	75 mg	6	10	6	30	100.0	26.0‡	74.0[B]	90
Nortriptyline	75 mg	6	10	6	120	100.0	62.5‡	37.5	90
Nortriptyline	75 mg	6	10	6	240	100.0	87.0‡	13.0	90
Paroxetine	60 mg	13	20	3	20	1005 ± 914.0[D]	unmeasurable*	100.0	91
Paroxetine	60 mg	13	20	3	40	1005 ± 914.0	unmeasurable*	100.0	91
Phenobarbital	200 mg	5	50	2	< 5	376 ± 31[H]	< 10*	100.0	75
Phenobarbital	200 mg	5	50	2	60	376 ± 31[H]	199 ± 56*	47.1	75
Phenylbutazone	200 mg	5	50	2	< 5	1647 ± 122[H]	30 ± 10*	98.2	75
Phenylbutazone	200 mg	5	50	2	60	1647 ± 122[H]	1154 ± 267*	29.9	75
Phenylpropanolamine	50 mg	7	25	2	5	1.62 ± 0.20[H]	0.57 ± 0.07*	64.8	74
Phenylpropanolamine	50 mg	4	0.5	1	0	80.0	42.0†	47.5[A]	19
Phenylpropanolamine	50 mg	4	5	1	0	80.0	5.2†	93.5[A]	19
Phenytoin	500 mg	6	50	2	< 5	357 ± 35[H]	2.8 ± 2.2*	99.2	81

Drug	Dose	n	Activated Charcoal Dose (g)	Form[a]	Delay[b] (min)	Bioavailability (Mean ± SD)[c,d] Control	Charcoal	Percent Reduction[e]	Ref
Phenytoin	500 mg	6	50	2	60	357 ± 35	79 ± 17*	77.9	81
Pindolol	10 mg	7	50	2	5	0.431 ± 0.065[H]	unmeasurable*	100.0	79
Piroxicam	20 mg	6	50	3	5	321.4 ± 96.0[F]	6.7 ± 7.3*	97.9	92
Propoxyphene	103 mg	6	50	2	5	3.65 ± 0.43[F,H]	0.15 ± 0.05‡	95.9	93
Quinidine	200 mg	6	50	2	5	17.6 ± 0.8[H]	umneasurable*	100.0	44
Salicylamide	1000 mg	4	1.5	1	0	92.5	71.8†	22.4[A]	19
Salicylamide	1000 mg	4	10	1	0	92.5	21.4†	76.9[A]	19
Salicylamide	750 mg	5	5	3	5	79.0	47.0	40.5[A]	5
Salicylate	975 mg	7	20	2	< 5	772.7 ± 333.6	479.7 ± 306.1†	37.9[C]	94
Salicylate	975 mg	7	20	3	< 5	772.7 ± 333.6	265.1 ± 127.0†	65.7[C]	94
Salicylate	1944 mg	12	60	4,6	60	96.3 ± 7.5	56.5 ± 12.5†	41.3[A]	95
Salicylate	260 mg	7	25	1	< 5	13274	6581*	50.4	96
Salicylate	260 mg	7	25	1	< 5	13274	8023*	39.6	96
Salicylate	260 mg	7	25	1	< 5	13274	8840*	33.4	96
Salicylate	260 mg	7	25	1	< 5	13274	9629*	27.5	96
Salicylate	1000 mg	4	1.9	1	0	99.7 ± 2.1	87.4 ± 1.9†	12.3[A]	97
Salicylate	1000 mg	5	10	1	0	99.7 ± 2.1	60.6 ± 2.2†	39.2[A]	97
Salicylate	1000 mg	5	10	1	60	99.7 ± 2.1	78.5 ± 9.2†	21.3[A]	97
Salicylate	1000 mg	5	10	1	180	99.7 ± 2.1	91.3 ± 2.4†	8.4[A]	97
Salicylate	975 mg	4	20	2	< 5	100.0	38.7 ± 10.5‡	61.3[A]	98
Salicylate	1000 mg	7	25	2	5	695 ± 66[H]	298 ± 20*	57.1	74
Salicylate	1000 mg	6	50	2	< 5	729 ± 72[H]	109 ± 28†	85.0	81
Salicylate	1000 mg	6	50	2	60	729 ± 72	546 ± 53*	25.1	81
Salicylate	1000 mg	6	25	2	< 5	940 ± 74[H]	218 ± 29*	76.8	87
Salicylate	1000 mg	6	25	2	60	940 ± 74[H]	701 ± 113*	25.4	87
Salicylate	500 mg	6	2.5	2	< 5	443 ± 55[H]	309 ± 42*	30.2	99
Salicylate	650 mg	3	50	2	< 5	456 ± 83	97.9 ± 36*	78.5[C]	100
Salicylate	972 mg	8	20	4	< 5	91.7 ± 4.7	62.3 ± 18.4*	32.1[A]	101
Salicylate	975 mg	8	10	3	0	94.2 ± 6.1	73.8 ± 6.1‡	21.7[A]	102
Salicylate	975 mg	6	15	1	30	846.5 ± 293.0	428.2 ± 218.6*	49.4	103
Salicylate	1500 mg	12	50	2	60	60.3 ± 13.3	52.5 ± 7.0*	12.9[A]	104

Salicylate	975 mg	10	10	2	< 5	98.6 ± 3.2	69.5 ± 6.8†	29.5[A]	105
Salicylate	972 mg	8	20	3	< 5	91.7 ± 4.7	62.3 ± 18.4*	32.1[A]	101
Salicylate	1000 mg	5	1.9	1	0	99.7	87.4†	12.3[A]	19
Salicylate	1000 mg	5	10	1	0	99.7	60.6†	39.2[A]	19
Salicylate	1000 mg SR	4	10	1	< 5	89.1 ± 7.7	63.2 ± 7.0†	29.1[A]	97
Salicylate	1000 mg EC	4	10	1	< 5	96.2 ± 6.0	71.2 ± 10.5†	26.0[A]	97
Salicylate	2925 mg EC	10	50	3,4	240	100.0	43.0†	57[B]	106
Sotalol	160 mg	7	50	2	5	64.3 ± 5.9[F,H]	0.5 ± 0.3*	99.2	107
Sulphadoxine	1500 mg	10	2	4	5	2533.0 ± 5.1[H,I]	1346.3 ± 85.2*	46.8	108
Tetracycline	500 mg	6	50	2	5	100.0	3.0*	97.0[B]	70
Tetracycline	500 mg	6	50	2	30	100.0	38.0*	62.0[B]	70
Theophylline	10 mg/k SR	5	1 g/kg	1	0	97 ± 4	38 ± 6†	60.8	109
Theophylline	500–600 mg	5	30	1	30	209.4 ± 23.6	74.3 ± 25.4*	64.5	110
Tilidine	44.2 mg	3	20	2	3	2.91 ± 1.21	0.31 ± 0.09†	89.3[C]	111
Tilidine	44.2 mg	3	20	2	25	2.91 ± 1.21	1.35 ± 0.53†	53.6[C]	111
Tolbutamide	500 mg	6	50	2	< 5	714 ± 53[H]	78 ± 22*	89.1	112
Tolfenamic acid	400 mg	6	25	2	< 5	18.6 ± 2.3[H]	2.29 ± 0.26*	87.7	87
Tolfenamic acid	400 mg	6	25	2	60	18.6 ± 2.3[H]	7.02 ± 2.08*	62.3	87
Tolfenamic acid	200 mg	6	2.5	2	< 5	9.50 ± 1.20[H]	0.33 ± 0.06*	96.5	99
Trimethoprim	200 mg	6	2.5	2	< 5	41.5 ± 7.3[H]	3.8 ± 0.9*	90.8	82
Trimethoprim	200 mg		10	2	< 5	41.5 ± 7.3[H]	1.0 ± 0.2*	97.6	82
Trimethoprim	200 mg		25	2	< 5	41.5 ± 7.3[H]	unmeasurable*	100.0	82
Trimethoprim	200 mg		50	2	< 5	41.5 ± 7.3[H]	unmeasurable*	100.0	82
Trimethoprim	200 mg		10	3	< 5	41.5 ± 7.3[H]	unmeasurable*	100.0	82
Valproate	300 mg	6	50	2	< 5	609 ± 71[H]	222 ± 58*	63.5	112

n = number of volunteers in study.

[a]1 = activated charcoal 900–1500 mg/m^2; 2 = activated charcoal 1600–2000 mg/m^2; 3 = unknown charcoal; 4 = with sorbitol; 5 = with saline cathartic; 6 = Medicoal.

[b]Delay (min) in giving charcoal after drug administration.

[c]AUC (m × h/mL) unless otherwise stated in comments.

[d]*$p < 0.05$; †$p < 0.01$; ‡$p < 0.001$; otherwise, not significant.

[A] = % urinary excretion of dose; [B] = % of control; [C] = recovered in urine (mg); [D] = ng × h/mL; [E] = μmol × h/mL; [F] = mmol × h/mL; [G] = mg × min/mL; [H] = data expressed as ± SEM; [I] = not crossover design.