

POSITION PAPER

## Position Paper: Cathartics<sup>#</sup>

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and European Association of Poisons Centres  
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### ABSTRACT

The administration of a cathartic alone has no role in the management of the poisoned patient and is not recommended as a method of gut decontamination. Experimental data are conflicting regarding the use of cathartics in combination with activated charcoal. No clinical studies have been published to investigate the ability of a cathartic, with or without activated charcoal, to reduce the bioavailability of drugs or to improve the outcome of poisoned patients. Based on available data, the routine use of a cathartic in combination with activated charcoal is not endorsed. If a cathartic is used, it should be limited to a single dose in order to minimize adverse effects of the cathartic. A review of the literature since the preparation of the 1997 Cathartics Position Statement revealed no new evidence that would require a revision of the conclusions of the Statement.

### 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.
- The two general types of osmotic cathartics used in poisoned patients are saccharide cathartics (sorbitol) and saline cathartics (magnesium citrate, magnesium sulfate, sodium sulfate).

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## RATIONALE

- Cathartics are intended to decrease the absorption of substances by accelerating the expulsion of the poison from the gastrointestinal tract. Since most drug absorption occurs rapidly in the upper GI tract, the use of cathartics is most likely to benefit patients who have ingested materials that are absorbed slowly. Few clinical poisons fit this profile. Slow-release products are a potential example, but there are little clinical data on the efficacy of cathartics. This review does not address whole bowel irrigation, a more aggressive form of purgation than the techniques discussed here.
- Sorbitol is often combined with activated charcoal as it improves the palatability of charcoal by imparting a sweet taste and by masking the grittiness of the charcoal.

## IN VITRO STUDIES

- A number of studies have investigated the effect of cathartics on the adsorption of drugs by activated charcoal.
- One study (1) evaluated the effect of magnesium citrate on the binding of salicylates to charcoal and found apparent pH-dependent changes in adsorption. At low pH, magnesium citrate interfered with salicylate adsorption and at high pH values it enhanced salicylate adsorption. The statistical significance of this increase was not calculated.
- Four other studies (2–5) have evaluated the impact of magnesium citrate, at controlled pH, on the adsorptive capacity of activated charcoal. At pH 1.2, magnesium citrate reduced the adsorptive capacity of charcoal by 15% ( $p < 0.05$ ) (2). In a study conducted at pH 4.0, magnesium citrate significantly ( $p < 0.01$ ) enhanced the adsorption of salicylate to charcoal, regardless of the initial salicylate concentration and the charcoal:salicylate ratio (3). In another study where the pH was unknown, but controlled, the presence of magnesium citrate apparently increased the adsorption of  $C^{14}$ -labeled paraquat at charcoal to paraquat ratios of 10:1 and 20:1 (4). A study using simulated gastric fluid with an unstated pH showed an apparent decrease in the adsorption of aspirin to charcoal when magnesium citrate was added and an apparent increase in adsorption to charcoal when simulated intestinal fluid was used (5).
- Adsorption of rifampicin and doxycycline on a commercial charcoal preparation (Ultracarbon, Merck) was investigated (6,7). The amounts of charcoal

ranging from 50 to 500 mg in a 5 mL solution, consisting of either drug in water or drug solution in sodium citrate or sodium chloride. These authors found that citrate increased the binding of rifampicin but decreased that of doxycycline, the findings being the opposite with saline.

## ANIMAL STUDIES

- The combination of magnesium citrate and activated charcoal given to mice 30 min after paraquat administration increased survival from 31% (controls) to 94% ( $p < 0.01$ ) (4).
- When sorbitol and mannitol were coadministered with activated charcoal to dogs, Van de Graaf, et al. (8) demonstrated that the area under the curve (AUC) for acetaminophen (paracetamol) was 75% greater with cathartics plus charcoal compared with charcoal alone ( $p = 0.07$ ) and the peak plasma acetaminophen concentration was 80.4% greater ( $p = 0.012$ ) after cathartics and charcoal compared with charcoal alone.
- In studies conducted in rats, the addition of activated charcoal to sorbitol reduced significantly the peak drug concentrations to 23.8% of control ( $p < 0.001$ ) for chlorpheniramine, to 20.6% of control ( $p < 0.001$ ) for chloroquine, to 25.6% of control ( $p < 0.001$ ) for pentobarbital, and to 55.2% of control ( $p < 0.001$ ) for aspirin (9).
- Sodium sulfate and activated charcoal administered to rats reduced significantly ( $p < 0.001$ ) peak plasma concentrations of salicylate, pentobarbital, chlorpheniramine, and chloroquine when compared with control. The combination was significantly ( $p < 0.001$ ) more effective than charcoal alone in reducing peak drug concentrations of salicylate, pentobarbital, and chloroquine (10).
- Sodium sulfate, but not sorbitol, together with superactivated charcoal increased survival (2 of 11) and significantly ( $p < 0.01$ ) increased survival times of rats that were given lethal doses of T-2 mycotoxin (11).

## VOLUNTEER STUDIES

### Cathartics Alone

- Magnesium sulfate did not alter significantly ( $p > 0.1$ ) the serum concentrations of lithium and salicylate when administered 30 min after dosing (12).

- Galinsky and Levy (13) showed that sodium sulfate did not change significantly the urinary recovery of acetaminophen (paracetamol) and its metabolites (mean±SD, 87.0±8.3%) when compared with control (89.6±10.7%). After the administration of sorbitol, urine salicylate recovery (95.9±14.4%) was not reduced significantly when compared to control (100%) (14).
- Al-Shareef, et al. (15) demonstrated that the mean peak plasma theophylline concentration (7.8 mg/L) was significantly ( $p<0.001$ ) greater in volunteers given sorbitol than in the control group (5.5 mg/L). The mean time to peak concentration was significantly ( $p<0.01$ ) shorter (11.38 h) in the sorbitol group than in the control group (16.0 h). There was no difference in the mean  $AUC_{0-24\text{ h}}$  between the sorbitol (116.6 mg/L/h) and control (97.6 mg/L/h) groups.
- In another study, Minton et al. (16) found sorbitol did not alter significantly the AUC of theophylline whether administered at 1 h (142.2 mg/L/h) or 6 h (124 mg/L/h) after dosing when compared with control (152.8 mg/L/h).

#### Sorbitol Plus Activated Charcoal

- Sorbitol and activated charcoal reduced significantly ( $p<0.01$ ) the AUC of theophylline ( $85.5\pm 10\text{ mg}\times\text{h/L}$ ) when compared with charcoal ( $113\pm 5.7\text{ mg}\times\text{h/L}$ ) and with no-treatment ( $304.6\pm 18.8\text{ mg}\times\text{h/L}$ ) groups (17).
- Keller et al. (18) found that sorbitol and activated charcoal reduced significantly ( $p<0.05$ ) salicylate elimination ( $0.912\pm 0.18\text{ g}$ ) in the urine when compared with charcoal alone ( $1.26\pm 0.15\text{ g}$ ).
- Al Shareef et al. (15) demonstrated that sorbitol and activated charcoal did not reduce significantly ( $p>0.05$ ) the AUC of theophylline (7.48 mg/L/h) when compared with charcoal alone (10.46 mg/L/h).
- Urinary salicylate excretion was not reduced significantly ( $p>0.05$ ) by the administration of sorbitol 43 g and activated charcoal 77 g (mean 63.8% and 61.5%, respectively) when compared to activated charcoal alone (mean 62.3%) (19).

#### CLINICAL STUDIES

- No clinical studies have been published to investigate the ability of cathartics, with or without activated charcoal, to reduce the bioavailability of drugs or to improve the outcome of poisoned patients.

## DOSAGE REGIMENS

### Sorbitol

- The dose of sorbitol is approximately 1–2 g/kg body weight. The conversion of milliliters of sorbitol to grams of sorbitol is as follows: sorbitol (70%) 100 mL =  $100\text{ mL}\times 0.7\times 1.285\text{ g sorbitol/mL (specific gravity)}=89.95\text{ g sorbitol}$ . The recommended dose is 70% sorbitol 1–2 mL/kg in adults and 35% sorbitol 4.3 mL/kg in children. These recommendations apply only to single doses of cathartics.

### Magnesium Citrate

- There are few dose-response data for magnesium citrate. A commonly recommended dose is magnesium citrate 10% solution 250 mL in an adult and 4 mL/kg body weight in a child.

## INDICATIONS

- Based on available data, there are no definite indications for the use of cathartics in the management of the poisoned patient.

## CONTRAINDICATIONS

- Absent bowel sounds, recent abdominal trauma, recent bowel surgery, intestinal obstruction, or intestinal perforation.
- Ingestion of a corrosive substance.
- Volume depletion, hypotension, or significant electrolyte imbalance.
- Magnesium cathartics should not be given to patients with renal failure, renal insufficiency, or heart block.
- Cathartics should be administered cautiously to the very young (<1 year of age) and to the very old.

## COMPLICATIONS

### Single Dose

- Nausea, abdominal cramps, vomiting.
- Transient hypotension.

### Multiple or Excessive Doses

- Dehydration.
- Hyponatremia in patients receiving sodium-containing cathartics.
- Hypermagnesemia in patients receiving a magnesium-containing cathartic.

## SUPPORTING DOCUMENTATION INTRODUCTION

In 1997 the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists published a position statement on the use of cathartics in the management of acute poisoning. This position statement concluded that the administration of a cathartic alone had no role in the management of poisoned patients and was not recommended as a method of gut decontamination.

Since that time, a number of publications have been produced in which there is reference to the use of cathartics in the management of poisoning. This manuscript is based on a literature review conducted in 2003 which examined publications from 1995 to establish whether there was further evidence of the benefits of this approach. Manuscripts were identified using searches of medical databases in which the key words "gut decontamination" and "cathartics" were used. Further searches were done using individual agents identified in these searches and known to be used clinically.

These papers were divided into the following groups: editorials and reviews; manuscripts describing clinical management involving case series; experimental studies; case reports; opinion surveys. Reviews were not used to form any opinion reflected in this position statement, but were included to ensure a full literature search had been completed. In addition, a number of case reports were identified in which cathartics were mentioned in the management of acute poisoning. The vast majority of these referred to the use of sorbitol in combination with activated charcoal. Since it was not possible to evaluate the efficacy of the use of sorbitol from these reports, they have not been discussed further.

A number of studies have been reported in the radiological and gastroenterological literature examining the efficacy of purgatives as preparations for colonic X-ray procedures and endoscopy. These report the effects of purgatives usually administered 24 h prior to such procedures and are therefore not directly relevant to decontamination in poisoning (20–24). One volunteer study (25) was identified in which the effects of two

cathartics (sodium and magnesium sulfate), metoclopramide 10 mg, propantheline and placebo were compared to the gastrointestinal transit of activated charcoal. This study did not examine the effects of these combination therapies on drug absorption.

The two general types of osmotic cathartics used in poisoned patients are saccharide cathartics (sorbitol) and saline cathartics (magnesium citrate, magnesium sulfate). Numerous cathartics (sodium phosphate, sodium sulfate, magnesium hydroxide, lactulose, mannitol, and castor oil) have been used in the past, but the administration of these agents is now less frequent. Polyethylene glycol is a cathartic agent, but is generally employed in the context of whole bowel irrigation. It is therefore not considered in detail in this review.

Data are limited regarding the mechanism of action of cathartics. Postulated mechanisms of action include a direct effect of the cathartic in the lumen of the intestines either promoting osmotic retention of fluid or extracting water from the intestinal circulation. The resulting increase in intraluminal contents activates gastrointestinal motility reflexes, which enhance the expulsion of the intraluminal contents.

## RATIONALE

The primary rationale for using cathartics is the belief that these agents reduce absorption of a poison by decreasing the time the poison or the poison–charcoal complex remains in the gut. Sorbitol improves the palatability of activated charcoal by imparting a sweet taste and by reducing the grittiness of activated charcoal. Although cathartics have sometimes been administered with activated charcoal to reduce the risk of constipation, there is no evidence that a single dose of activated charcoal produces constipation.

## IN VITRO STUDIES

### Saline Cathartics

Cooney and Wijaya (1) measured the effect of pH on the binding of sodium salicylate to charcoal. At pH 1.2, magnesium citrate was primarily present (99.6%) in the undissociated form, which binds well to charcoal. At pH 1.25 and at a charcoal:drug ratio of 3.3:1, the addition of varying concentrations of magnesium citrate to the solution reduced the amount of sodium salicylate adsorbed to charcoal from approximately 85% to approximately 73%. At pH 9, magnesium citrate occurred primarily (99.3%) in the

dissociated form, which adsorbs poorly to charcoal. Following the addition of varying concentrations of magnesium citrate to the solution at pH 9, the amount of sodium salicylate adsorbed to charcoal increased from approximately 25% to 40%. No data tables or statistical analyses were reported in this study.

Czajka and Konrad (2) studied the effect of magnesium citrate 5.9% (0.13 M), sodium sulfate 8.52% (0.6 M), and magnesium sulfate 7.22% (0.6 M) on the adsorption of aspirin to activated charcoal at pH 1.2. The premixing of magnesium citrate with activated charcoal reduced the adsorptive capacity of the activated charcoal by 15% ( $282.71 \pm 5.91$  mg aspirin/g charcoal) ( $p < 0.05$ ) compared with the control of distilled water ( $332.35 \pm 14.35$  mg aspirin/g charcoal). There was no significant difference in adsorptive capacity between the mixture that contained magnesium sulfate ( $320.08 \pm 9.87$  mg aspirin/g charcoal) or sodium sulfate ( $329.94 \pm 3.38$  mg aspirin/g charcoal) and the control of distilled water. This study demonstrated no desorption of aspirin from the drug-charcoal complex at acid pH by any of these mixtures.

The results of a study by Ryan et al. (3) indicated that citrate ions and, to a lesser extent, magnesium ions were responsible for the significant ( $p < 0.01$ ) enhancement of the adsorption of salicylate to activated charcoal compared with control (activated charcoal 100 mg in water 30 mL). The pH of all test solutions was adjusted to pH 4 to eliminate the effect of pH on adsorption. At the three initial concentrations of salicylate tested, the percent salicylate adsorbed to activated charcoal in magnesium citrate compared with the percent salicylate adsorbed in water (control) were: at salicylate 200 mg/L, 100% vs. 51%; at salicylate 600 mg/L, 82.5% vs. 33.3%; and at salicylate 1000 mg/L, 60% vs. 21.4%.

The addition of magnesium citrate 2.4 mL and simulated gastric fluid 12 mL changed the adsorption of aspirin 40 mg to charcoal 400 mg from 40 mg to 39.5 mg and 36.7 mg, respectively. The addition of 2.4 mL and 12 mL magnesium citrate to simulated intestinal fluid increased the adsorption of aspirin to charcoal from 31.5 mg to 35.3 mg and 34.2 mg, respectively (5). No statistical analyses were reported in this study.

Gaudreault et al. (4) examined the effect of magnesium citrate at an unknown, but controlled, pH on the adsorption of  $^{14}\text{C}$  paraquat to activated charcoal. At a charcoal to paraquat ratio of 10:1, the presence of magnesium citrate increased adsorption from 37% to 53%. When the ratio was increased to 20:1, the percent bound increased from 56% to 86%. No ranges were reported for these data and no statistical analyses were provided for these comparisons.

A group from Nigeria has studied the effects in vitro of cathartic solutions on the efficacy of charcoal (6,7). Adsorption of two specific compounds was studied, rifampicin and doxycycline. A commercial charcoal preparation (Ultracarbon, Merck) was placed in a test tube with a drug solution, the solution being 5 ml and the amounts of charcoal ranging from 50 to 500 mg. Solutions consisted of either drug in water or drug solution in sodium citrate or sodium chloride. These authors found that citrate increased the binding of rifampicin but decreased that of doxycycline, the findings being reversed with saline.

The significance of in vitro experiments for the treatment of human poisoning is unclear since cathartic solutions would necessarily have to pass through the acidic content of the stomach and their pH might therefore change. No consistent pattern of interaction is observed with drug-to-drug variation.

### Sorbitol and Mannitol

Van de Graaff et al. (8) demonstrated that adsorption isotherms for acetaminophen (paracetamol) and activated charcoal in simulated gastric (pH=1.2) and intestinal (pH=6.9) fluids were not altered significantly by the addition of sorbitol or mannitol. The mean decrease in binding capacity was  $-2 \pm 7\%$ , suggesting that sorbitol and mannitol do not interfere with the adsorptive capacity of activated charcoal.

Al-Shareef et al. (15) added sorbitol 2 g to a charcoal slurry 1 g. This combination significantly ( $p < 0.05$ ) increased the binding of aminophylline to charcoal from 642 mg/g to 735 mg/g after incubation at 37°C and pH 7.4.

Nakamura and colleagues (26) carried out an in vitro study of the interaction between sorbitol and a range of activated carbons (charcoal) and their ability to bind acetaminophen. In this experimental model, both the equilibrium amount adsorbed and the removal rate of acetaminophen decreased with increasing sorbitol concentration. The authors did not perform an in vivo study and the sorbitol concentrations ranged between 5% and 50% weight-volume. These concentrations are likely to be far in excess of those seen in vivo. This article indicates that excessive use of sorbitol should be discouraged.

### Polyethylene Glycol

Atta-Politou et al. (1998) (27) studied the interaction between polyethylene glycol lavage solution (PEG-ELS) and the adsorption of fluoxetine onto activated charcoal (Carbomix (Norit, Netherlands) and "pure" activated charcoal powder (Merck) in vitro.

The slurries were incubated in two environments, one acid (pH 1.2) and one neutral (pH 7.2) to mimic different intestinal conditions. Polyethylene glycol and charcoal were added either together or separately to fluoxetine solutions. In either instance the addition of the polyethylene glycol solution reduced significantly fluoxetine absorption. The authors advise against combining polyethylene glycol and activated charcoal in the management of fluoxetine poisoning. This effect did not appear to be pH-dependent.

## ANIMAL STUDIES

### Cathartics Alone

Four studies have evaluated the effect of the administration of cathartics alone on bioavailability (AUC), peak drug concentrations, or survival rates. However, all of these studies used doses of the cathartics that exceeded therapeutic recommendations and none used intervals between the ingestion and administration of cathartic that are common in the treatment of poisoned patients; consequently, the clinical relevance of any positive results is questionable.

Gaudreault et al. (4) used groups of 16 male mice to study the effects of magnesium citrate on survival following paraquat administration. Compared with a survival rate of 31% in male mice receiving paraquat 200 mg/kg, the administration of magnesium citrate 10 mL/kg 30 min after the intragastric administration resulted in a survival rate of 69%, which was not a statistically significant difference.

In a study (8) of groups of 17 dogs, the administration of mannitol 2 g/kg and sorbitol 2 g/kg immediately after intragastric insertion of acetaminophen 600 mg resulted in a 31% decrease ( $p=0.002$ ) in the  $AUC_{0-11\text{ h}}$  for acetaminophen. The maximum plasma acetaminophen concentration was reduced by 15%. This was not statistically different ( $p=0.17$ ) when compared with control (water alone).

Groups of 7–15 rats were given sorbitol (70%) 20 mL/kg immediately after gastric instillation of aqueous suspensions of chlorpheniramine 80 mg/kg, chloroquine 100 mg/kg, pentobarbital 50 mg/kg, and aspirin 100 mg/kg (9). Compared with controls (no treatment), sorbitol reduced the peak drug concentrations to 62.4% for chlorpheniramine ( $p<0.001$ ), 65.5% for chloroquine ( $p<0.05$ ), 50.4% for pentobarbital ( $p<0.001$ ), and 80.9% for salicylates ( $p<0.001$ ). The administration of sorbitol reduced the AUCs of chlorpheniramine, chloroquine, and pentobarbital to

68.2%, 69.0%, and 40.6% of control, respectively. No statistical analyses were reported for comparison.

Sodium sulfate (1.32 mg/kg in water 20 mL/kg) administered concurrently with aspirin 100 mg/kg to rats (7–10 per group) reduced the peak plasma salicylate concentration by 16.6% ( $p<0.05$ ) but administration of sodium sulfate did not produce significant reduction in peak plasma concentrations of pentobarbital, chlorpheniramine, or chloroquine (10). Results of the AUC for these groups were presented neither numerically nor analyzed statistically.

### Cathartics Plus Activated Charcoal

Survival rates were measured in groups of 16 mice that were administered magnesium citrate (10 mL/kg body weight) and activated charcoal 4 g/kg 30 minutes after dosing with paraquat 200 mg/kg (4). Rats administered magnesium citrate and activated charcoal had a survival rate of 94% compared with a survival rate of 31% ( $p<0.01$ ) in control animals.

Van de Graaff et al. (8) investigated the effect of saccharide cathartics and activated charcoal in nine dogs following the administration of acetaminophen (paracetamol) 0.6 g/kg. The AUC of acetaminophen was 75% greater ( $p=0.07$ ) after the administration of mannitol 2 g/kg and sorbitol 2 g/kg with activated charcoal 3 g/kg than with activated charcoal alone. The peak plasma acetaminophen concentration was 80.4% greater ( $p=0.012$ ) in dogs that received activated charcoal plus cathartics than in those treated only with activated charcoal. There were no adjustments for fluid or electrolyte imbalances.

Sorbitol 20 mL/kg (70%) and activated charcoal in charcoal:drug ratios of 2–4:1 were administered to groups of 7–10 rats immediately after dosing with chlorpheniramine 80 mg/kg, aspirin 100 mg/kg, pentobarbital 50 mg/kg, and chloroquine 100 mg/kg (9). Sorbitol and activated charcoal significantly reduced the peak tissue drug concentrations (percent of control) to 23.8% ( $p<0.001$ ) for chlorpheniramine, to 20.6% ( $p<0.001$ ) for chloroquine, to 25.6% ( $p<0.001$ ) for pentobarbital, and to 55.2% ( $p<0.001$ ) for aspirin. Data for AUC were not analyzed statistically.

A significant ( $p<0.001$ ) reduction in the peak plasma concentrations was observed following the administration of aspirin 100 mg/kg, pentobarbital 50 mg/kg, chlorpheniramine 80 mg/kg, and chloroquine 100 mg/kg to groups of 7–10 rats immediately after dosing with sodium sulfate 1.32 g/kg and activated charcoal (10). The combination of sodium sulfate and activated charcoal was more effective than activated charcoal alone in reducing the peak drug concentrations of salicylate,

pentobarbital, and chloroquine ( $p < 0.001$ ). Sodium sulfate plus charcoal did not apparently alter the peak concentration of chlorpheniramine compared to the charcoal-only group. The ratio of activated charcoal to drug was 2:1 for pentobarbital and chloroquine, and 4:1 for aspirin and chlorpheniramine.

Survival times and rates were measured in a study of rats given lethal doses of T-2 mycotoxin together with sorbitol 0.35 g/kg, sorbitol 2 g/kg, or sodium sulfate 1 g/kg and superactivated charcoal in doses of 0.04, 0.1, 0.15, 0.175, 0.20, 0.50, and 1.0 g/kg (11). Two of 11 rats in the sodium sulfate and charcoal group survived, whereas none of the rats in the sorbitol group survived; two rats of ten in the charcoal-alone group survived. The median effective dose of activated charcoal was 0.175 g/kg. The survival times of the rats in the cathartic group were significantly less ( $p < 0.01$ ) than survival times in the charcoal-only group. There were no adjustments for fluid and electrolyte imbalance.

The extrapolation of these animal studies remains limited by the following: the clinical relevance of the statistical difference in systemic absorption between the combination of activated charcoal and cathartics and activated charcoal alone; the time of treatment in relation to drug ingestion, biochemical (i.e., water solubility, ionization) and physiological differences between experimental conditions and clinical situations; and the power of the study to detect a difference in systemic absorption between activated charcoal and the combination of activated charcoal and cathartic.

## VOLUNTEER STUDIES

### Cathartics Alone

Magnesium sulfate 30 g did not alter significantly ( $p > 0.1$ ) the serum lithium and salicylate concentrations after the administration of lithium 600 mg and aspirin 1500 mg to 10 adults 30 min after dosing (12).

Aspirin 975 mg was administered to four adults, followed immediately by sorbitol (70%) 100 mL (14). Aspirin recovery was assessed in urine. Control treatment was assumed to have a 100% recovery. Compared to control, sorbitol resulted in  $95.9\% \pm 14.4\%$  recovery (might be worth commenting on the limitations of this study—how they accounted for amounts in excess of 95.9%) of the aspirin dose in the urine. This amount was not different statistically from control. The limitations of this study are the sample size and assumptions on accuracy of recovery in the control subjects.

Eight adults received acetaminophen 1 g followed by sodium sulfate (USP) 4.5 g at intervals of 0, 2, 4, and 6 h (12). The urinary recovery of acetaminophen plus metabolites, as a percentage of the total dose, was measured. Sodium sulfate administration resulted in the recovery of  $87.0 \pm 8.3\%$  compared with  $89.6 \pm 10.7\%$  in the control group. The difference was not statistically significant.

Sorbitol (70%) 50 mL was administered to eight adults at 6, 14, and 20 h after the administration of slow-release theophylline 600 mg (15). The mean plasma theophylline concentration was significantly ( $p < 0.001$ ) greater in the sorbitol group (7.8 mg/L) than in the control group (5.5 mg/L). The mean time to peak concentration was significantly ( $p < 0.01$ ) shorter (11.38 h) in the sorbitol group compared to control (16.0 h). There was no difference ( $p > 0.05$ ) in the mean  $AUC_{0-24 \text{ h}}$  between the sorbitol (116.6 mg/L/h) and control (97.6 mg/L/h) groups.

Sorbitol (70%) 150 mL, was administered to 10 adults 1 and 6 h after ingestion of sustained-release theophylline 600 mg (as three 200 mg tablets) and 16 radiopaque placebo tablets (16). No significant difference was observed in  $AUC_{0-36 \text{ h}}$  in the sorbitol 1-h (142.2 mg/L/h) and 6-h (124.0 mg/L/h) groups compared with control (152.8 mg/L/h). The mean placebo tablet recovery was greater than control [1.5 (range 0–14)] in both the 1-h [5.5 (range 0–16)] and 6-h [13.5 (range 4–19)] groups.

Sorbitol (70%) 75 mL, was administered at 6 and 8 h after dosing with sustained-release theophylline 1.2 g to nine adults (17). Superactivated charcoal 20 g was given at 6, 7, 8, 10, and 12 h after theophylline administration. There was a significant difference ( $p < 0.01$ ) in the mean  $AUC_{6-30 \text{ h}}$  between the sorbitol and charcoal ( $85.5 \pm 10 \text{ mg} \times \text{h/L}$ ), and charcoal ( $113 \pm 5.7 \text{ mg} \times \text{h/L}$ ) and control groups ( $304.6 \pm 18.8 \text{ mg} \times \text{h/L}$ ).

Sorbitol 1.5 g/kg and activated charcoal 25 g were administered to 10 adults 1 h after dosing with aspirin 2.5 g (18). The 48-h urinary excretion of salicylate in those receiving aspirin and activated charcoal with sorbitol was significantly less ( $p < 0.05$ ) ( $0.912 \pm 0.18 \text{ g}$ ) when compared with those who received aspirin and activated charcoal alone ( $1.26 \pm 0.15 \text{ g}$ ).

The addition of sorbitol (70%) 50 mL to activated charcoal 20 g administered 2, 8, 14, and 20 h after the ingestion of sustained-release theophylline (600 mg) by eight adults did not reduce ( $p > 0.05$ ) the mean  $AUC_{0-24 \text{ h}}$  (7.48 mg/L/h) compared with charcoal alone (10.46 mg/L/h) (15).

The addition of sorbitol (70%) 43 g or 77 g to activated charcoal 20 g administered immediately after

**Table 1.** Transit time (time to first stool) vs. AUC as a % of control for cathartic and activated charcoal (C+AC) and activated charcoal alone (AC).

	Mean transit time (h)		AUC (mg/L/h) as % of control		Ref.
	C+AC	AC	C+AC	AC	
Cathartic					
Magnesium citrate	7.0	22.0	37* (Salicylate)	43	(19)
			7* (Atenolol)	9	(19)
			47* (Phenylpropanolamine)	35	(19)
Sodium sulfate	4.2	45.7	73.1* (Salicylate)	50.6	(20)

\*Not significantly different from activated charcoal alone.

ingestion of aspirin 972 mg by eight adults did not alter ( $p>0.05$ ) the mean 72-h urinary excretion of salicylate [mean 63.8% (43 g) and 61.5% (77 g), respectively] compared with the use of activated charcoal alone (mean 62.3%) (19). The mean excretion in the control group was 91.7%.

A study of eight healthy volunteers given acetaminophen (paracetamol) 3 g (28) compared the effect of administering activated charcoal 50 g in sorbitol (70%) 183 g at 1 h after ingestion with activated charcoal 50 g at 1-h postingestion. The corrected mean  $AUC_{0-8\text{ h}}$  for charcoal alone was 86.58 mg/L/h (70.5% of control) compared with 90.85 mg/L/h (74% of control) for the combination ( $p>0.05$ ). The study contained a serious methodological flaw in that the two groups received activated charcoal preparations with different surface areas (950 m<sup>2</sup>/g vs. 1500 m<sup>2</sup>/g).

### Transit Time

The use of cathartics with activated charcoal reduced the transit time of the charcoal-laden stool through the gut (29,30), but this reduction in transit time has not been associated with significantly reduced drug absorption (Table 1).

In volunteers, the mean transit time of charcoal-laden stool without cathartics averages about 24–30 h (31,32) with a range of 7.8–56.7 h (33,34). The administration of sorbitol resulted in mean transit times ranging from 0.9–8.5 h (31,35–37). The administration of magnesium citrate resulted in mean transit times ranging from 3–14 h (29,31,34,36,37) and the mean transit time for magnesium sulfate, was 9.3 h (31) and for sodium sulfate, 4.2–15.4 h (30,32).

When used in therapeutic doses, anticholinergic drugs do not appear to alter the efficacy of cathartics as exemplified in a study of 40 adult subjects who received clidinium bromide (37). The drug did not alter significantly the mean onset (4.5 h vs. 6.3 h)

or the duration (48.5 h vs. 62.3 h) of charcoal-laden stool compared with the use of activated charcoal 15 g and magnesium citrate 300 mL alone. The ingestion of large amounts of drugs that slow intestinal motility (38) also slowed sorbitol-induced transit time (19.6 h) compared with the ingestion of drugs that did not affect motility (4.7 h) ( $p<0.05$ ).

### Hazards of Cathartics

Since the last systematic review, additional papers have been published that indicated the potential hazards of magnesium salts used as a treatment for constipation (39), or a preoperative bowel preparation in the context of renal failure (40). Qureshi and Melonakos (41) reported the same complication in a patient with normal renal function. Pitcher and colleagues (42) reported fatal hypocalcemic hyperphosphatemia in a patient given sodium phosphate enemas.

### Unusual Use of Cathartics

Treble and Thompson (43) reported the use of cathartics to increase clearance from the gut of spent air rifle pellets. In this case blood lead levels were elevated to 56 µg/dL (2.7 µmoles/L) but the patient was asymptomatic. In more serious poisoning, chelation therapy would have been a more appropriate option in association with gut decontamination (44,45).

### INDICATIONS

Based on available experimental and clinical data, there are no definite indications for the use of cathartics in the management of the poisoned patient. If used, a cathartic should be limited to a single dose in order to minimize the adverse effects of the cathartic.



## DOSAGE REGIMENS

### Sorbitol

The dose of sorbitol is approximately 1–2 g/kg body weight. The conversion of milliliters of sorbitol to grams of sorbitol is as follows: sorbitol (70%) (100) mL = 100 mL  $\times$  0.7  $\times$  1.285 g sorbitol/mL (specific gravity) = 89.95 g sorbitol. The recommended dose is sorbitol (70%) 1–2 mL/kg in adults and sorbitol (35%) 4.3 mL/kg in children. These recommendations apply only to single doses of cathartics.

### Magnesium Citrate

There are few dose-response data for magnesium citrate. A recommended dose of 10% magnesium citrate solution is 250 mL for an adult and 4 mL/kg for a child.

## CONTRAINDICATIONS

The use of cathartics is contraindicated in the presence of absent bowel sounds, intestinal obstruction or perforation, recent bowel surgery, volume depletion by hypotension, significant electrolyte imbalance, or ingestion of a corrosive substance. Cathartics should be used cautiously in the very young (<1 year of age) or the very old.

## COMPLICATIONS

### Single Dose

#### Sorbitol

In healthy adults, the administration of sorbitol (70%) 150 mL produced no significant changes in serum sodium ( $p=0.16$ ) or serum phosphorus ( $p=0.258$ ) concentrations 4 h after ingestion (35). Adverse effects from the administration of therapeutic doses of sorbitol include vomiting (36,46), abdominal cramps (17,18,35), nausea (17,18,28), diaphoresis (17), and transient hypotension (17). In some studies no adverse effects were reported (15).

#### Magnesium Citrate

Adverse effects are uncommon after single, therapeutic doses of magnesium citrate in healthy subjects. In a group of young (age 1–5 years) children

with suspected ingestions of toxic substances who were given magnesium citrate 233 mg/kg, the frequency of vomiting was approximately 17% (36).

#### Magnesium Sulfate

The administration of magnesium sulfate 13.9 g did not produce significant elevations of serum magnesium in seven healthy adult volunteers (47). A second study of patients presenting to an emergency department with an overdose confirmed the lack of clinically significant elevation of magnesium concentrations in healthy adults following the administration of standard, single doses of magnesium sulfate. There were no statistically significant differences in baseline serum magnesium from serum magnesium 1 h and 4 h after the ingestion of magnesium sulfate 30 g (48). Vomiting was observed in 17% of children given magnesium sulfate 250 mg/kg (36).

## Multiple or Excessive Doses

Serious adverse reactions including dehydration and electrolyte imbalance (hypermagnesemia, hypernatremia) may occur in patients receiving multiple doses of sodium- or magnesium-containing cathartics. Patients with renal dysfunction are at increased risk (36,49). Hyponatremic dehydration may be caused by excessive doses of sorbitol.

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