# Influence of Prokinetics on the Gastrointestinal Transit and Residence Times of Activated Charcoal

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## Abstract

**Objective:** To find the effects of prokinetics, saline cathartics and different charcoal doses on the gastrointestinal transit and residence times of activated charcoal (AC).
**Setting:** Five undergraduate volunteers of College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria, were studied.
**Methods:** After an overnight fast, the volunteers were given lOg and 20g AC with and without saline cathartics, in a simple cross-over design in which the subjects served as their own control. In another experiment, the volunteers received lOg AC and magnesium sulphate, with propantheline (as bromide 15mg), metoclopramide (as hydrochloride 10mg), placebo liquid or identical placebo capsule. Gastrointestinal transit and residence times of AC were recorded.
**Results:** Increase in the dose of AC significantly ($P<0.05$) decreased the transit, but not the residence time of AC. Addition of saline cathartics (Na2SO4 and MgS04) decreased both the transit and residence times of AC significantly ($P<0.05$). Also, administration of propantheline, but not metoclopramide, produced a significant ($P<0.05$) decrease in both the transit and residence times of AC. The transit and residence times were statistically ($P<0.05$) different in both the magnesium sulphate group, as well as in the placebo liquid and placebo capsule groups.
**Conclusion:** Cathartic efficiency is enhanced by alteration of gastrointestinal motility with propantheline (JPMA 52:354; 2002).

## Introduction

Activated charcoal (AC) has been used in the management of poisoning for more than 150 years[1]. The goal of using AC is to decrease systemic absorption of poisons, thereby reducing toxicity. Although AC avidly adsorbs toxic substances, this process has not been demonstrated to be irreversible[2].The quicker a poison passes through the gastrointestinal tract, the less will be its desorption, provided that hyper peristalsis and increased fluid secretion do not facilitate desorption. There is an unsubstantiated claim that cathartic enhanced propulsion of charcoal-poison complex improves the antidotal efficacy of AC[3-5]. Propantheline is a synthetic anticholinergic agent, which has been used for gastrointestinal disorders where its motility slowing and spasmolytic effects are considered beneficial. With an oral dose of 30mg propantheline has been shown to delay gastric emptying by 100% in all subjects[6]. Metoclopramide acts as a gastrointestinal prokinetic agent, speeding up gastric emptying and increasing peristalsis mainly in the small intstine[7]. In the clinical setting, the use and elimination of AC can be affected by agents with anticholinergic, narcotic, or sedative-hypnotic properties of the ingested substance, because they cause decreased bowel activity[8].
The purpose of this study was to examine the influence of modification of gastric emptying AC

quantity and effect of saline cathartics on the gastrointestinal or oroanal transit and residence times of AC.

## Methods

Five healthy volunteers (2 women and 3 mend between the ages of 25 and 38 years (mean age 32 year) and weighing 60-85 kg (mean 78 kg) participated in the study after giving their informed consent. Subjects were nonsmokers and did not take alcoholic beverages before or during the study. The Human and Toxicological Ethics Committee of our institution approved the study.

### Experimental Design

The study used a simple crossover design in which subjects served as their own control. Activated charcoal (AC) (Ultra Carbon, Merk), sodium chloride (USP) magnesium sulphate (USP) and sodium sulphate (USP) were all freshly prepared with sterile injection water. Gastric emptying was experimentally modified by use of 15mg propantheline bromide and 10mg metoclopramide hydrochloride. Gastrointestinal transit and residence times were determined after administration of each of the preparations (Tables 1 and 2).

The volunteers were instructed to fast from solid foods for 12 hours before ingestion of AC saline cathartic mixtures. The volunteers continued fasting for the 2 hours post-test dosing, but were asked to record volume of water taken during this fast period. The volunteers recorded the time at which the test dose was administered and the time of first appearance of AC in faeces (transit time) and the time the last trace of charcoal was found in faeces (residence time). A one-week wash-out period separated each of the phases (Tables 1 and 2).

**Table 1. Effect of activated charcoal quantity and saline cathartics on gastrointestinal transit and residence time of AC.**

| Phase | Treatment |
|---|---|
| 1 | Activated charcoal (10g) in aqueous slurry (350 ml) control |
| 2 | Activated charcoal (20g) in aqueous slurry (350 ml) control |
| 3 | Activated charcoal (10g) in aqueous slurry (350 ml) with 30 ml of 50% sodium sulphate solution |
| 4 | Activated charcoal (20g) in aqueous slurry (350 ml) with 30 ml of 50% sodium sulphate solution |
| 5 | Activated charcoal (10g) in aqueous slurry (350 ml) with 30 ml of 50% sodium chloride solution |
| 6 | Activated charcoal (20g) in aqueous slurry (350 ml) with 30 ml of 50% sodium chloride solution |

**Table 2. Effect of magnesium and gastric emptying on the gastrointestinal transit and residence times of AC.**

| Phase | Treatment |
|---|---|
| 1 | Activated charcoal (10g) in aqueous slurry (350 ml) with 30 ml of 50% magnesium sulphate solution |
| 2 | Activated charcoal (10g) in aqueous slurry (350 ml) with 30 ml of50% magnesium sulphate and 15 mg propantheline (PP). |
| 3 | Activated charcoal (10g) in 350 ml of placebo liquid with 30 ml of 50% magnesium sulphate. |
| 4 | Activated charcoal (10g) in aqueous slurry (350 ml) with 30 ml of 50% magnesium sulphate and placebo capsule (PC) |
| 5 | Activated charcoal (10g) in (350 ml of ) placebo liquid (PL) and placebo capsule (PC) |
| 6 | Activated charcoal (10g) in aqueous slurry (350 ml) with 30 ml of 50% magnesium sulphate (MS) and 10 mg metoclopramide (MP) |

The differences between sample mean were analysed using Student's t-test for paired data, with statistical significance defined as $P<0.05$. The results are expressed mean±S.E.M. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 8.0 software package.

**Results**

The mean gastrointestinal transit and residence times of the various treatment protocols are shown in Figure.

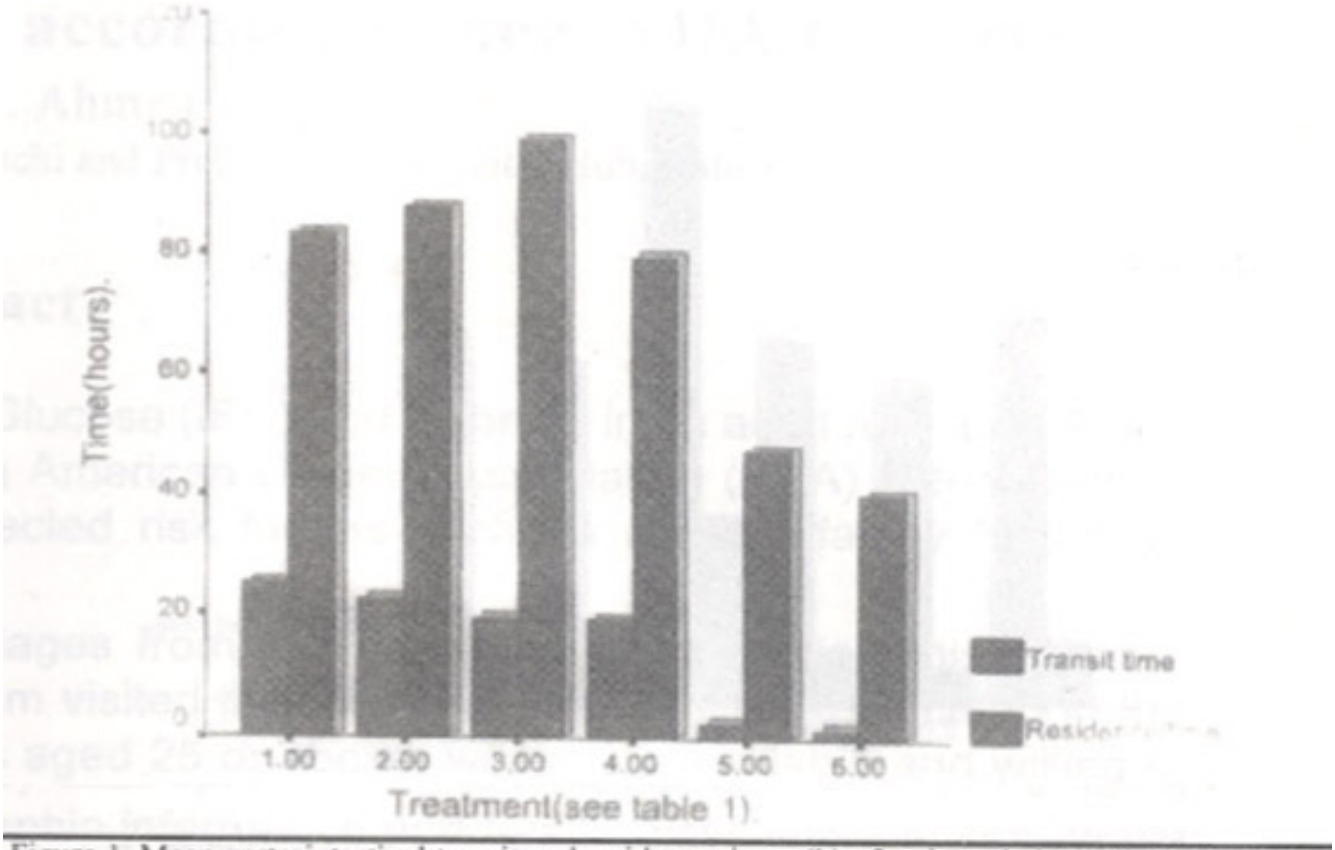


Figure 1. Mean gastrointestinal transit and residence times (h) of activated charcoal administered alone (control) and with saline cathartics.

The mean transit times after administrations of lOg and 20g AC were 25.49±0.90h (range 24.05-27.15) and 22.78±0.61h (21.57-23.20) respectively. Increase in AC dose (from 10-20) significantly ($P<0.05$) increased the transit time of AC. The average residence times were 83.47±6.93h (75.15-96.05) and 87.66±7.66h (72.30-96.00) respectively. The differences in the residence times for lOg and 20g were nonsignificant ($P>0.05$). The volunteers reported mild gastrointestinal upsets, dryness of throat and dehydration, which increased with AC quantity. The stool was firm.

Administration of sodium chloride with lOg and 20g AC significantly ($P<0.05$) reduced the transit time from 25.49+0.90h to 19.56±0.70h and 19.34+1.65h respectively. Sodium chloride increased significantly ($P<0.05$) the residence time from 83.47±6.93h to 99.18±3.01h in the lOg AC group. There was, however, a non-significant ($P>0.05$) reduction in residence time from 83.47±6.93h to 79.57+6.92h in the 20g AC group. The volunteers complained of dehydration and polydypsia, which resulted in intake of 1,500 to 3,000 ml of water within the first 6h of treatment. The stool was slightly firm.

There was slight gastrointestinal discomfort with slightly firm stool and polydypsia after administration of $Na_2SO_4$. The gastrointestinal transit and residence times were all significantly ($P<0.05$) reduced in the 10 and 20g with $Na_2SO_4$ treated groups.

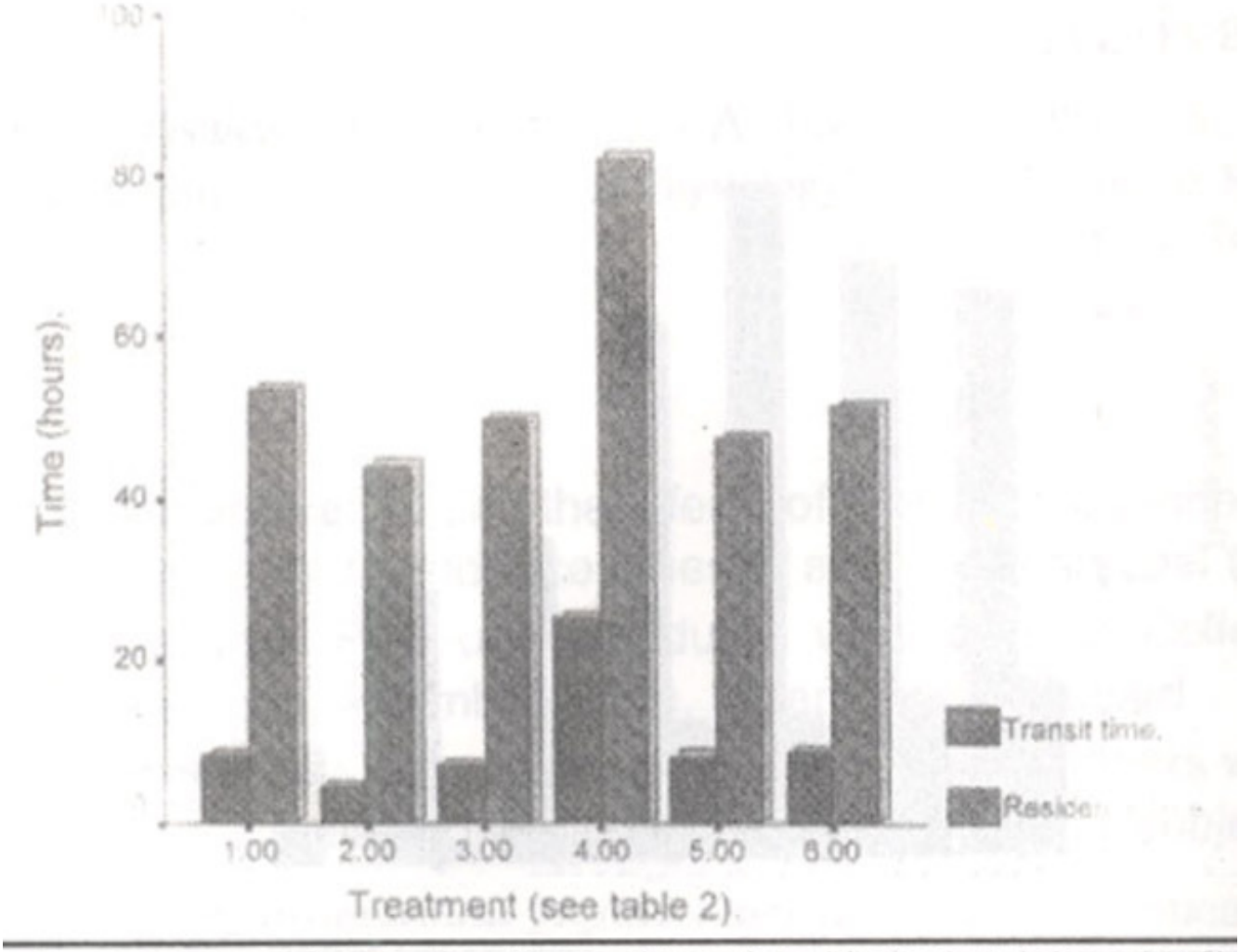


Figure 2. Mean gastrointestinal transit and residence times (h) of activated charcoal (AC) administered with magnesium sulphate (MS) alone (control), with propantheline (PP), metoclopramide (MP), placebo liquid (PL) and placebo capsule (MP).

Figure 2 shows the effect of $MgSO_4$ in shortening the gastrointestinal transit and residence times of AC in the presence of propantheline and metoclopramide. Administration of propantheline or metoclopramide produced a significant ($P<0.05$) difference in the transit but not the residence time of AC. The transit and residence times were statistically increased in the combined $MgSO_4$, AC, placebo liquid and placebo capsule group.

**Discussion**

In our previous study[9], which suggested potential benefit .of some saline cathartics in poison management, we also recommended further studies on the influence of treatment upon a marker substance. The resent study investigated the effects of AC quantity, saline catharics (sodium chloride, sodium sulphate and magnesium sulphate) and drugs that alter gastrointestinal motility on transit and residence times of AC. Two pharmacological agents (ropantheline for slowing down and metoclopramide for speeding up gastric emptying) were used. Although solutions ingested in the study were blinded to eliminate bias, other factors that influence gastric motility such as stress and physical activity were not controlled.

It is evident from this study that increase in charcoal quantity produced a significant ($P<0.05$) reduction in the gastrointestinal (oro-anal) transit time and statistically equal residence time. Administration of sodium chloride produced slower gastrointestinal transit time compared to sodium sulphate. This observation is in agreement with our earlier finding[9]. Gastric emptying rate and residence time within the small intestine are conventionally believed to be important determinants affecting the rate and extent of drug absorption[10]. In the average, transit time in healthy adults is approximately 94 min (range 50-120 min) in small bowel[11] and 45h (range 25-150h) in the whole gut[12]. In this study, alteration of gastrointestinal motility by propantheline shortened significantly ($P<0.05$) the transit and residence times of AC. On the other hand, no significant effects were observed on either the transit or residence time, after the administration of metoclopramide. Propantheline and metoclopramide are known to act on the gastrointestinal differences were observed, in gastrointestinal transit and residence times, between the drug treatments.

Although the gastrointestinal tract is long, certain changes in the upper gastrointestinal tract affect the entire length. An investigation and analysis of the influence of propantheline on the effect of magnesium sulphate on gastrointestinal transit and residence times of AC revealed that there were significant reductions. These results support previous studies[13] on the effect of cathartics on the excretion of AC and suggest that anticholinergic drugs, when used at therapeutic doses, do not inhibit cathartic efficiency. The only clinical side effect detected with the propantheline was dryness of the mouth in all volunteers. This lasted for few hours and at no instance was it accompanied by other anticholinergic manifestations.

Physiological factors such as phases of the menstrual cycle were disregarded in the assessment of transit and residence times, because the influence of hormonal factors such as gastric emptying and bowels transit and residence times is slight and obviously of no clinical importance[14].

In conclusion, cathartic efficiency on the gastrointestinal transit and residence times of AC, appear to be enhanced by alteration of gastrointestinal motility with propantheline, when therapeutic doses are used. It appear also, that increase in charcoal dose shortens the gastrointestinal transit time of AC.

**References**


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