A STUDY OF THE EFFECTS OF MAGNESIUM TRISILICATE INGESTION IN HUMANS

by

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INTRODUCTION

The silicates of magnesium have been long known in medicine, being mentioned by Dioscorides[1] in his Materia Medica. A few have been used as delicacies or as famine foods. Some of those existing in natural states are Forsterite, Serpentine, Cyanite, Aphrodite, Talc, and Meerschaum. The latter term, meaning sea foam, is indicative of its color and porosity, and is applied to the naturally occurring trisilicate of magnesium.

Hutch[2] of England introduced synthetic hydrated magnesium trisilicate to the medical profession in 1936 as an antacid for treating peptic ulcer. In in vitro experiments he found that at temperatures and acidities approaching physiological conditions there is a definite speeding up of the neutralization reaction as the temperature rises, but the gradient is not a steep one. In an experiment in which he used one gram of trisilicate, an amount less than equivalent to the hydrochloric acid used, he noted fast neutralization involving about 45 per cent of the magnesium content of the trisilicate. This occurred in about 15 minutes. Following fast neutralization, 31 per cent of the trisilicate was used up in the next hour, and all but 6 per cent had been utilized at the end of three hours. The slow stage of neutralization occurred independent of the particle size or the degree of hydration of the trisilicate. Powder kept under water for a week showed about the same course of neutralization.

Hutch[3] also measured the adsorptive power of hydrated magnesium

trisilicate. He found that it effectively adsorbs a variety of materials, such as acid and basic dyes, alkaloids, bacterial toxins, putrefactive amines, pepsin and food poisons. An interesting selective action was noted in that it adsorbs basic dyes more efficiently than acidic ones, and also readily removes muscarine but not the poison of amanita phthalloides from solution.

Gastric juice from a test meal corresponds approximately to N/20 hydrochloric acid. Hydrated magnesium trisilicate reacts with hydrochloric acid according to the following equation:

$$Mg_2Si_3O_8 + 4HCl \rightarrow 2MgCl_2 + 3SiO_2 + 2H_2O$$

Magnesium trisilicate is insoluble in water. The silica (SiO_2) resulting from such reaction is also insoluble. The total antacid effect is essentially equivalent to the magnesium content of the trisilicate. The slowness at which neutralization occurs is of peculiar clinical interest.

After the ingestion of magnesium trisilicate the small intestine receives a magma of hydrated silica in a gel condition mixed with trisilicate which escaped decomposition because of the neutralization lag mentioned above. The soluble magnesium chloride formed is converted to insoluble magnesium hydroxide at the alkaline pH of the small intestine.

Occasionally magnesium trisilicate produces a laxative effect.(5) Magnesium chloride formed in the stomach operates osmotically as a saline aperient in the bowel. The different responses of various individuals may be due to several factors. Personal susceptibility no

doubt plays a part. The amount of chloride formed depends on the amount of silicate given, the acidity and volume of the gastric contents, and the rate of flow through the pylorus. The amount of magnesium chloride remaining in solution decreases as the alkalinity of the intestinal juice increases. The final amount of chloride in the lower part of the bowel is influenced by the reaction of the ileum and colon. Should their contents be acid, magnesium hydroxide and carbonate will pass into solution as salts and by osmotic effect act as an evacuant.

The neutralization of hydrochloric acid by magnesium trisilicate may be due to two separate phenomena, namely, chemical neutralization and adsorption. Neutralization in the chemical sense produces magnesium chloride and silica. Adsorption binds the acid to the surface of the trisilicate or silica. In order to evaluate the two processes W.N. Mann (6) devised the following experiment. To a known weight of ignited magnesium trisilicate he added normal hydrochloric acid representing 14 per cent excess over that required for complete reaction according to the above equation. Interaction was allowed to continue for a fixed time, and the amount of acid remaining unneutralized was determined by rapid back titration with standard sodium hydroxide, using phenolphthalein as indicator. The endpoint of the titration was difficult to establish because the color faded rapidly due to the solution quickly becoming acid upon standing. This latter fact suggests that the recurring acidity of the solution was due to the liberation of adsorbed acid from the surface of the trisilicate. Determinations of the quantity of acid neutralized by adsorption were

made for different times of interaction. It was found that the over-all process of neutralization takes place rapidly at first, followed by a sharp decrease in rate. The fast phase of reaction neutralized 92 per cent of the available acid, this occurring in fifteen minutes. In order to determine what part of this 92 per cent of acid was neutralized by chemical action with magnesium trisilicate, the above experiment was repeated, the solution being filtered after twenty minutes. The amount of hydrochloric acid chemically neutralized was determined from the magnesium content of the filtrate. This proved to be 70 per cent of the equivalent amount of acid present, the remaining 22 per cent of acid being neutralized by adsorption.

Mutch (7) assumed that since the antacid power is sustained for hours even in the presence of excess acid, that not only is hyperchlorhydria controlled, but also it furnishes a basis for local antacid therapy in the floor of the ulcer itself. Magnesium trisilicate acquires a gelatinous consistency, and if any should deposit in the ulcer crater it will progressively neutralize the acid which diffuses through it. This should also establish a local zone free of peptic activity, even when digestion is proceeding freely in other parts of the stomach, since pepsin is one of the substances easily adsorbed by magnesium trisilicate.

The purpose of this thesis has been to determine the effect if any, of magnesium trisilicate given orally, upon the magnesium and calcium levels of the blood and urinary excretion.

Much investigation has been done upon the effect of various soluble magnesium salts upon the magnesium level of blood and urine, but surprisingly little is known relative to the effect of magnesium trisilicate, in spite of the fact that it is widely used in medical practice.

Magnesium is an important constituent of the body for it is universally present, being found chiefly in bones and muscles. There is a close relationship between calcium and magnesium, but their relative distribution is widely divergent. Normally magnesium tends to be higher than calcium in soft tissue, and calcium higher than magnesium in extracellular tissue and bone. Magnesium acts as a coenzyme in many of the enzyme systems of the body, such as phosphatase. According to Lohmann a small amount is combined with adenylpyrophosphate present in muscle.

Hawk and Bergeim[8] state the blood serum level of magnesium to be normally 1.0-3.0 mgms. in 100 cc. of serum, with an average of 2.0 mgms. Greenberg and associates[9] found the average to be slightly higher, about 2.74 mgms. Tibbetts and Aub,[10] and Watchorn and McCance[11] concluded that it was between 2.3 and 2.6 mgms. The daily urinary excretion of magnesium is usually between 0.1 and 0.2 gms.[8], the amount depending upon the diet. Approximately 50 per cent of the excreted magnesium

is eliminated by the kidneys, and 50 per cent in the feces. Tibbetts and Aub (10) claim that 60 per cent is found in the feces and that from 80 to 85 per cent may be present when the intake of magnesium is increased.

Cagood (12a) considers the normal calcium range of blood serum to be 9.0-12.0 mgms. per 100 cc., while several other authors claim it to be 9.0-11.5 mgms. The daily output of calcium in the urine, depending on the nature of the diet, averages about 0.1-0.3 gms. From 10-40 per cent of the calcium excreted is eliminated by the kidneys, but this is not a dependable absorption index since calcium salts may be reexcreted into the intestine after absorption. This fact is also true for magnesium. Experiments like those of Renvall's, quoted from Mendell and Benedict (14), actually contain more magnesium than is introduced into the alimentary tract with the diet, indicating an endogenous source of magnesium. This was especially true in cases where the magnesium content of the diet was low.

The state of magnesium in blood serum has been studied by Hatchorn and McCance (11), and Greene and Powers (16). Stary and Winternitz, quoted from Schmidt and Greenberg (15), first showed that about 70 per cent of the serum magnesium was diffusible by the method of compensation dialysis. In this method the procedure is to dialyze serum against a saline solution equivalent in kind and amount to the salts contained in blood excepting for the specific ion under investigation. This ion is varied until the level is obtained at which there is no further alteration produced by the exchange between serum and salt solution. An alternative method is by

ultrafiltration in which the serum is filtered through a collodion membrane by applying pressure. Using this latter method Watchorn and McCance[11] found the diffusible magnesium of human serum to be about 80 per cent of the total.

It is generally reported from compensation dialysis analyses that some 60-70 per cent of the serum calcium is diffusible. Murray[17] and Zucker[18] have reported figures of this magnitude for normal human blood. By ultrafiltration the range is from 40-60 per cent.

Since the work of Rona and Takahashi, quoted from Schmidt and Greenberg[15], it has been widely held that non-diffusible calcium exists in combination with plasma proteins. In 1925 Nichols and Sterling, quoted from Schmidt and Greenberg[15], demonstrated that under certain conditions a part of the non-diffusible fraction might also exist in the form of colloidal calcium phosphate. The non-diffusible magnesium very likely combines with serum proteins in a manner similar to calcium, but probably does not form a colloidal magnesium phosphate.

The calcium-magnesium ratio in the body is variously given by different authors. McCrudden[19] in experiments on normal dried bone found it to be 200:1. Von Euler and Rydborn, quoted from Mendell and Benedict[14], claim a ratio of 240:1 in normal bone ash. Morgulis[20], analyzing the bone ash of different animals, found that it varied with the species, the ash of bones of dogs and rabbits having a calcium-magnesium ratio of 72:1.

From the variable concentration ratios of calcium and magnesium in different tissues one may obtain approximate evidence as to the

source of these elements in the excretions. If demineralization involves the bones the calcium-magnesium ratio will be high, whereas the reverse if true in loss of the elements from soft tissues.

Mendell and Benedict[14] were the first to associate the output of magnesium with that of calcium. They injected magnesium sulfate and magnesium chloride parenterally into dogs, cats, and rabbits, and demonstrated the importance of the kidneys in the elimination of excess magnesium. They observed an increased output of calcium in the urine in these experiments, and reversely, an increased concentration of magnesium upon injection of calcium chloride. It was noted that a considerable quantity of the excess of both calcium and magnesium salts injected were retained for some time in the body. Diuresis followed the injection of all of these solutions.

Several workers have shown that magnesium is related to irritability of muscles. Meltzer and Auer[21] demonstrated this action very effectively in the intact animal by parenteral injection of magnesium salts into rabbits and monkeys. In concentrations up to 0.1-0.8 gms. per kilogram of body weight they could produce a profound narcosis and anesthesia, and in larger amounts could produce death. It was shown that the condition probably is related to the magnesium concentration in the serum. A mild sedative effect may be obtained when the serum level reaches 5 mgms. per 100 cc. At a level of 18-21 mgms. profound coma is produced. Similar results were obtained by Meltzer and Wallace[22] in dogs. In their opinion a similar relation

holds for man so that a serum concentration of 5-6 mgms. per cent is necessary to give a mild sedative action. Taylor and Winter (23) determined 7-11 and 18-21 mgms. per cent respectively to be the levels for light and deep narcosis in rabbits. They criticize the sedative level given by Neuwirth and Wallace (22) since they failed to find even light narcosis when the serum magnesium of dogs was 10 mgms. per cent.

Meltzer and Auer (21) discovered the interesting "waking action" of calcium salts upon magnesium anesthesia. As indicated above, the anesthetic limits of magnesium salts are between 0.1 and 0.2 gms. per kilo of weight when given subcutaneously. This dose varies somewhat in different animals. Higher doses than the upper limit are usually fatal. However, by giving calcium salts during the anesthesia, animals have been known to survive doses as large as 0.3 gms. per kilo. These workers proposed no theory for this relation of calcium and magnesium. However, Yamawaki (15), upon studying these effects, arrived at conclusions which might possibly represent the true explanation. He pointed out that magnesium narcosis is essentially due to action on the central nervous system, as suggested by the general anesthesia, loss of reflexes, removal of vagal inhibition of the heart, and in terminal stages a continuous fall in blood pressure and paralysis of respiration. The loss of the standing reflex, and unconsciousness point to an involvement of the medulla oblongata. He was of the opinion that the counteracting effect of calcium was also of central nervous system origin. In other words the "waking action" of calcium salts on magnesium narcosis in his estimation is not due to any

physiological antagonism, but rather to individual action upon different parts of the brain. Calcium chloride produces irritability in the upper brain and in the corpus striatum, and this could be the cause of the antinarcotic action. Stransky[15] studied the calcium and magnesium contents of the blood of rabbits into which magnesium sulfate was injected subcutaneously in sufficient amounts to cause the narcosis described by Meltzer and Auer.[21] He noted a definite lowering of the serum calcium, and since the magnesium level was raised, a fall in the calcium-magnesium ratio. He attributes the narcosis to this latter fact.

Studies of the effects of the ingestion of magnesium salts on calcium retention give more variable results than those concerned with injection. Malcolm[24] in 1905 increased the urinary calcium in dogs by feeding them magnesium chloride. Hart and Steenbock[25] fed magnesium chloride and magnesium sulfate to pigs, and obtained increased urinary but not fecal calcium. These workers noticed that when soluble phosphates are given with the magnesium salts, the loss of calcium decreased. This work has been confirmed by Schutte, Hoklas, and Palmer[26] with cattle. They gave the cattle 155-165 gms. of Epsom salts ($MgSO_4 \cdot 7H_2O$), and markedly lowered the calcium balance of the animals on phosphorus deficient rations. Addition of phosphorus corrected the deleterious effect of the magnesium salts.

Studies on humans have shown only slight variations in urinary magnesium with increased magnesium intake. Givens[27] placed nine healthy

adults on a natural food diet containing more magnesium than calcium. After a preliminary day on this diet the urine was collected for three days. Then an excess of calcium was provided by adding milk and calcium salts to the diet, and the urine collected for another three days. In only three of the nine individuals was the urinary magnesium found to be greater than the calcium, and this was only transitory. In general, throughout the experiment more calcium than magnesium was excreted in the urine, or if such was not the case, the usual calcium-magnesium ratio could be brought about by the ingestion of milk. Bogert and McKittrick (28) devised an experiment in which they placed four young women on a uniform diet low in calcium. Then after four days they added six gms. of magnesium citrate per day to the diet. This increased the urinary and fecal magnesium in all four cases, the urinary and fecal calcium in three out of four cases, and the total calcium in all cases. Next they added six gms. of calcium lactate per day to the basic rations, causing increased urinary and fecal calcium in all four individuals.

Grace Medes (29), after determining normal magnesium, calcium and phosphorus on a series of normal rats by an ashing process, put other series of rats on diets varying in the above elements. She found that on a low calcium diet there was a decrease in magnesium and calcium but no effect on the phosphorus content, while on a high calcium routine there was an increase in calcium and phosphorus, but a slight decrease in magnesium; on a low phosphorus diet all three elements

were decreased but on a high phosphorus diet normal growth occurred; on a low magnesium diet the calcium and phosphorus were increased and the magnesium slightly decreased, while on rations high in magnesium there was no effect on calcium and phosphorus, but a slight increase in magnesium. She concluded from these experiments that the composition of rats is more constant in respect to magnesium under varying conditions than to calcium and phosphorus.

In a recent paper, Haag and Palmer, (30) using growth as the index of changes in mineral metabolism showed a suppressing effect of magnesium at some levels of calcium and phosphorus ingestion in rats. In similar experiments Kinslie and Steenbock (31) found that excessive amounts of magnesium salts in rat rations, resulted in loss of appetite and severe digestive disturbances, so that any specific effect of magnesium on calcium relations was masked. Upon giving smaller amounts which were however, relatively large, such disturbances were not manifested. Under these conditions no effect on calcium metabolism was demonstrable by additions of magnesium salts to food very deficient in calcium or to rations having sufficient calcium.

Farquharson, Salter, Tibbetts and Aub (32) studied the effect of the ingestion of ammonium chloride upon patients on a fixed low calcium diet and on a high calcium diet. The calcium excretion was found to vary with the total excess acid eliminated and appeared to be independent of the reaction of the urine. The quantitative increase in calcium excretion in response to ingestion of acid was greatly influenced by the basal level of calcium excretion as well as by the amount of excess

acid ingested.

Page, Heffner and Frey (33) have made some recent investigations upon the urinary excretion of silica in humans following the oral administration of magnesium trisilicate. First they determined the average twenty-four hour excretion of silica on a regular diet over a period of days. This they found to be 16.3 mgms. Then five gms. of synthetic hydrated magnesium trisilicate were given to each subject in five spaced doses for four consecutive days. The total amount of trisilicate ingested was 20 gms., and contained approximately 9.2 gms. of silica. The increased silica excretion in the urine during the course of the experiment averaged 484 mgms., so that a rough approximation of the amount of silica excreted in the urine from the magnesium trisilicate taken orally is about 5.2 per cent.

EXPERIMENTAL

The primary objects of this investigation were to study the effect of the ingestion of magnesium trisilicate upon blood and urine magnesium and upon the over-all digestion-absorption processes for proteins, fats, and carbohydrates.

Because of a possible influence of the blood magnesium level upon blood calcium and urinary calcium excretion, serum and urine calcium determinations were run simultaneously with the magnesium analyses.

The people used for these experiments were kept on their usual diets but were cautioned not to take any calcium or magnesium salts during the period of experimentation. Calcium and magnesium determinations were run on fasting blood serum and twenty-four hour urine samples for five days previous to trisilicate ingestion in order to establish normal values. Each individual was then put on a routine of two grams of Mallinckrodt's magnesium trisilicate three times a day between meals, spaced approximately at 10:30 AM, 2:30 PM, and 10:30 PM. Calcium and magnesium in fasting blood serum and twenty-four hour urine specimens were determined for a consecutive period of four or five days on this routine, or until the concentration of these two elements returned to the level previous to ingesting the magnesium trisilicate. Any unusual symptoms such as diarrhea and sleepiness during this period were recorded.

A high gastro-intestinal acidity increases the absorption of calcium and also the excretion of calcium in the urine. In order to

determine whether gastro-intestinal acidity and magnesium are similarly related the pH and titretable acidity of urine samples were run daily. The diet in each case was kept relatively constant, the articles of food and portions of each being about the same each day. After this "normal" period each person took two grams of magnesium trisilicate to three times a day as before, and urine and feces were collected and analyzed.

METHODS OF ANALYSIS

Blood. All analyses were done on blood samples collected daily before breakfast.

Urine. Urine was collected in 24 hr. samples and preserved with toluene.

Feces. Each 24 hr. sample was diluted to 1000 cc. with 10 per cent sulfuric acid, mixed well and allowed to stand overnight to further emulsification.

A. Calcium in Serum.

The Clark-Collip Modification of the Kramer-Tisdall Method (34) was used.

Reagents. Ammonium Oxalate Solution, 4 per cent.

Ammonium Hydroxide, 2 per cent.

Normal Sulfuric Acid.

N/100 Potassium Permanganate prepared from N/10 stock solution.

N/100 Sodium Oxalate prepared from N/10 stock solution, used to standardize the permanganate solution.

Procedure. 2 cc. of clear serum were placed in a graduated 15 cc. pyrex centrifuge tube. 2 cc. of distilled water, and 1 cc. of 4 per cent ammonium oxalate solution, were added and the contents of the tube mixed thoroughly. The mixture was allowed to stand 1 hr. with occasional agitation, and then centrifuged for 5 minutes at 1500 revolution per

minute. The supernatant liquid was carefully poured off into another container and the tube allowed to drain for 5 minutes on a filter paper. After wiping the mouth of the tube the precipitate was stirred up and the sides of the tube washed with about 3 cc. of 2 per cent ammonia water, in a fine stream from a wash bottle. The suspension was centrifuged and drained as before. 2 cc. of normal sulfuric acid were blown from a pipette upon the precipitate to break up the mat and facilitate solution. The tube was placed in a boiling water bath for one minute and immediately titrated with N/100 potassium permanganate to a definite pink color which persisted for at least 1 minute. If necessary during the titration the tube was placed in the water bath to raise the temperature to between 70 and 90 degrees.

Calculations. 1 cc. of N/100 potassium permanganate is equivalent to 0.2 mgms. of calcium.

$$(x-b) \times 0.2 \times \frac{100}{2} = \text{mgms. of calcium per 100 cc. serum.}$$

x = cc. of permanganate required for titration.

b = blank = cc. of permanganate required to titrate 2 cc. of sulfuric acid solution to the usual end point.

B. Calcium in Urine.

The same procedure was used as for blood serum. If the urine was neutral or alkaline, the entire sample was made slightly acid to litmus (after determining the pH and titratable acidity), by adding a few drops of concentrated hydrochloric acid. A small portion of

this was filtered and 1 cc. of the filtered urine, 3 cc. of distilled water and 1 cc. of ammonium oxalate were mixed for precipitation of the calcium.

Calculations. $\frac{(x-b) \times 0.2 \times 24 \text{ hr. urine volume}}{1000}$ = gms. of calcium.

C. Magnesium in Serum.

A modified Denis Method was used.(35)

Reagents. Ammonium Phosphate solution containing 5 cc. of concentrated ammonia per liter.

Dilute ammonia, 1 part ammonia to 2 parts distilled water.

Molybdate-Sulfuric Acid Reagent.

2.5 gms. ammonium molybdate in 100 cc. of 5 N sulfuric acid.

Reducing agent.

1 gm. Amidal (2,4-Diaminophenol Dihydrochloride) in 100 cc. of 20 per cent solution of sodium bisulfite.

Stock standard phosphate solution. 0.4386 gms. pure dry monopotassium phosphate per liter.

Working standard. 10 cc. of stock standard were diluted to 100 cc. 3 cc. = 0.0195 mgms. of magnesium.

75 per cent alcohol containing 10 cc. concentrated ammonia per liter.

Procedure. 3 cc. of supernatant fluid from the calcium determination were pipetted into a graduated 15 cc. pyrex centrifuge tube. 0.5 cc. of ammonium phosphate solution and 2 drops of concentrated ammonium hydroxide were added and the tube agitated. After standing over night the solution was centrifuged at about 1800 revolutions per minute for 10 minutes. Then the supernatant fluid was siphoned off, taking care not to disturb the precipitate. The best siphon for this was found to be a narrow glass tube slightly curved up at the end. This tube was connected to a suction pump. The precipitate and sides of the tube were washed with 5 cc. of dilute ammonia, centrifuged and siphoned off again. This was repeated a second and third time, and then washed with 5 cc. of alcohol solution, and centrifuged. The alcohol was siphoned off and the tube was allowed to stand in a warm place until the ammonia had evaporated.

The magnesium ammonium phosphate formed was dissolved in 1.5 cc. of molybdate reagent. 0.3 cc. of reducing agent were added, the mixture diluted to 15 cc. and mixed well. 3 cc. of working standard were placed in another tube with 1.5 cc. of molybdate reagent and 0.3 cc. of reducing agent, mixed well and diluted to 15 cc. The colors were read in a Klett-Summerson photoelectric colorimeter.

Calculations. 3 cc. of supernatant fluid corresponds to 1.2 cc. of serum.

$$\frac{\text{Reading of unknown} \times 0.0195 \times 100}{\text{Reading of standard} \times 1.2} = \text{mgms. of}$$

magnesium per 100 cc. of serum.

D. Magnesium in Urine.

3 cc. of the supernatant fluid from the urine calcium were used and treated in the same way as for blood magnesium.

Calculations. $\frac{\text{Reading of unknown} \times 0.0195 \times \text{24 hr. urine volume}}{\text{Reading of standard} \times 0.6 \times 1000} =$ gms. of magnesium.

E. Titrable Acidity of Urine.

The method used was as given in the Laboratory Outline of Biochemistry.(36)

Reagents. 30 per cent Potassium Oxalate Solution.

N/10 Sodium Hydroxide.

Procedure. 25 cc. of urine were pipetted into an erlenmeyer flask and 3 cc. of potassium oxalate solution and 2 drops of 0.2 per cent phenolphthalein added. The mixture was titrated with N/10 sodium hydroxide.

Calculations. $\frac{\text{cc. of sodium hydroxide used} \times \text{volume of 24 hr. urine}}{25} =$ cc. of N/10 acid present in 24 hr. urine.

F. pH of Urine.

The pH was determined on filtered urine with a Beckman pH Meter.

G. pH of Feces.

0.5 gm. of well mixed feces were emulsified in 5 cc. of distilled water and filtered. The pH of the filtrate was determined with a

Beckman pH Meter.

II. Determination of Nitrogen in Feces by the Kjeldahl Method.

I. Digestion of Feces.

Reagents. Digestion Mixture. 50 per cent sulfuric acid containing 150 gms. anhydrous potassium sulfate and 5 cc. of selenium oxychloride per liter.

Anhydrous Sodium Sulfate.

Procedure. 5 cc. of emulsified feces mixture described previously were placed in a 12 inch pyrex test tube with 10 cc. of digestion mixture, 1 gm. of anhydrous sodium sulfate and a boiling rod. The test tube was supported in a vertical position with a burette clamp on a ring stand. The mixture was heated as rapidly as possible but cautiously until all tendency toward foaming stopped. At the same time the sides of the tube were kept hot enough with another burner to prevent the condensation of steam. When all of the water was boiled off and white fumes began to ascend in the tube, the latter was covered with a glass bulb and the micro-burner adjusted so that a maximum rate of refluxing was maintained without forcing acid fumes outside the tube. The mixture was boiled gently for 20-30 minutes after it had become clear.

Dilution. This digest was quantitatively washed into a 50 cc. volumetric flask and diluted to the mark with distilled water.

II. Determination of Nitrogen in the Feces Digest.

The procedure used was a distillation method as given in the Laboratory Outline of Biochemistry.(36)

Reagents. N/70 Sulfuric Acid.

N/70 Sodium Hydroxide.

40 per cent Sodium Hydroxide.

Procedure. 5 cc. of the diluted digest prepared above were placed in a 12 inch pyrex test tube and connected to a distilling head, the delivery tube of the latter being just immersed beneath the surface of 25 cc. of N/70 sulfuric acid in a 12 inch test tube. 10 cc. of distilled water and 10 cc. of 40 per cent sodium hydroxide were slowly added to the digestion mixture through a side tube fitted with a short length of rubber tubing and a screw clamp which was closed tightly immediately after adding the base. The contents were mixed well, cautiously brought to a boil, and kept boiling until sodium sulfate started to crystallize out of the mixture. The receiving tube was removed from the distilling apparatus, and the delivery tube rinsed into the acid. The unneutralized acid was titrated with N/70 sodium hydroxide, using 3 drops of methyl red and 3 drops of methylene blue (Tashiro's) as indicator.

Calculations. Each cc. of N/70 sulfuric acid is equivalent to 0.2 mgms. of nitrogen.

25 - cc. of N/70 sodium hydroxide used x 0.2 x 2000 = mgms. nitrogen in sample.

I. Determination of Nitrogen in Urine by the Kjeldahl Method.

The method used was the same as for feces.

Reagents. Same as for feces.

Procedure. 5 cc. of urine were diluted to 200 cc. 5 cc. of this solution were placed in a 12 inch pyrex test tube with 3 cc. of digestion mixture and about 0.25 gm. anhydrous sodium sulfate. The mixture was heated over a micro-burner as in the digestion of feces. Boiling was continued for 10 minutes after the solution had cleared. The mixture was then allowed to cool to room temperature and the tube fitted to the distilling head. 10 cc. of water and 10 cc. of 40 per cent sodium hydroxide were added slowly through the side tube and screw clamp closed tightly. The contents were mixed well, and the ammonia carefully distilled over into 25 cc. of N/70 sulfuric acid. The unneutralized acid was titrated with N/70 sodium hydroxide using Toshiro's indicator.

Calculations. 5 cc. of a 1 to 40 dilution of urine is equivalent to 0.125 cc.

$$\frac{25 - \text{cc. of N/70 sodium hydroxide used} \times 0.2 \times \text{24 hr. urine vol.}}{0.125 \times 1000} =$$

gms. of nitrogen in 24 hr. sample.

J. Determination of Fermentable Sugar in Feces After Acid Hydrolysis.

1. Acid Hydrolysis and Preparation of Filtrate.

An iron filtrate was prepared according to the method of Steiner, Urban and West.(37)

Reagents. 25 per cent Ferric Sulfate.

Barium Carbonate

Reagents continued.

Sulfuric Acid C.P.

Procedure. 50 cc. of feces in 10 per cent sulfuric acid were diluted to 200 cc. (giving 0.5 N acid) and gently boiled under reflux for 5 hrs. The solution was cooled and diluted to 500 cc. 85 cc. of this solution were placed in a 500 cc. Erlenmeyer flask with 15 cc. of ferric sulfate solution and mixed well. About 90 gms. of barium carbonate were added in small portions with shaking until most of the carbon dioxide was expelled. The flask was then stoppered and shaken vigorously and the pressure released repeatedly until no more carbon dioxide evolved. The mixture did not redden blue litmus. The solution was filtered under light suction on a Büchner filter. The filtrate was made acid to congo red paper by the addition of 2-3 drops of concentrated sulfuric acid and filtered.

II. Fermentation of Filtrate.

The filtrate was fermented according to the method of Curtis and West.(38)

Reagents. 15 per cent suspension of Fleishmann's yeast.

Procedure. 5 cc. of yeast suspension were centrifuged, the supernatant liquid decanted and the sides of the centrifuge tube and top of the yeast layer wiped with a small roll of filter paper. About 10 cc. of filtrate were added to the yeast tube, mixed well with the yeast and allowed to ferment at room temperature for 15 minutes with

occasional stirring. After centrifugation, the filtrate was decanted through a small filter.

III. Analysis of Filtrate for Fermentable Substances.

Method used was that of the Laboratory Outline of Biochemistry.[36]

Reagents. Shaffer-Hartmann-Somogyi Reagent.[39]

	Gms. per liter.
Anhydrous Sodium Carbonate	25
Sodium Bicarbonate	20
Rochelle Salts	25
Copper Sulfate with 5 moles of water	7.5
Potassium Iodate (20 cc. of 1 N solution)	0.856
Potassium Iodide	1.0

Iodide-Oxalate Reagent.

2 per cent potassium iodide containing 2.5 per cent potassium oxalate.

Normal Sulfuric Acid.

Sodium Thiosulfate 0.005 N, prepared from N/10 stock solution.

1 per cent starch solution.

Procedure. 5 cc. samples of the fermented and unfermented filtrate, each in duplicate, were pipetted into 25 x 200 mm. pyrex tubes, 5 drops of 0.02 per cent phenol red added, and 0.3 N sodium hydroxide until the indicator turned red. 5 blanks of 5 cc. of

distilled water and phenol red were also prepared. After the addition of 5 cc. of sugar reagent to the tubes, they were covered with glass bulbs and heated in an actively boiling water bath for 15 minutes. The tubes were then cooled to about 30 degrees C. in a vessel of water, each, followed by 5 cc. of 1.0 N sulfuric acid quickly blown in. Each tube was shaken with bulb in place, until the precipitate of cuprous oxide had dissolved. After standing 5-10 minutes the sides of the tubes and the glass bulbs were washed down with a fine stream of water from a wash bottle. Titrations were made with thiosulfate, 2 drops of 1 per cent starch solution being added near the endpoint.

Calculations. Calculations were made in terms of glucose reducing equivalents. 1 cc. of thiosulfate titration is equivalent to 0.113 mgms. of glucose.

0.425 cc. of the original feces mixture was present in each sample.

$$\frac{\text{Fermented filtrate titration} - \text{Unfermented filtrate titration} \times 0.113 \times 1000}{0.425 \times 1000}$$

gms. of fermentable reducing substance in total sample.

K. Determination of Fat in Feces.

The Saxon Method as outlined in Hawk and Bergeim was used.(8)

Reagents. Concentrated hydrochloric acid.

Ether.

95 per cent Alcohol.

Low boiling Petroleum Ether, leaving no detectable residue upon evaporation.

Procedure. 5 cc. of the acid feces mixture were placed in a 100 cc. glass stoppered graduated cylinder. 1 cc. of concentrated hydrochloric acid was added and sufficient distilled water to make a total of 30 cc. Exactly 20 cc. of ether were added, and the cylinder stoppered, and shaken vigorously for 5 minutes. This was allowed to stand for a few seconds, and then exactly 20 cc. of 95 per cent alcohol were added and the cylinder again shaken for 5 minutes. This was permitted to stand for a short time to allow the ether, containing practically all of the fat, to separate. The ether layer was blown off into a 150-200 cc. beaker. This was accomplished in the same manner that water is blown from a wash bottle, using an upward bent tube placed at the ether-water junction. The thin layer of ether which remained was diluted with 5 cc. of ether, the cylinder slightly agitated, and the ether blown off. This was repeated 5 times, care being taken each time to wash down the sides of the cylinder. The stopper was also washed.

20 cc. of ether were again added and the cylinder shaken for 5 minutes and set aside. When the ether had nearly stratified, it was blown off and washed 5 times as before.

The ether-alcohol solution was evaporated until no trace of the alcohol remained. 30 cc. of low-boiling petroleum ether were added and the mixture allowed to stand over night.

The petroleum ether solution of the fat was filtered

and the filter paper washed well with petroleum ether. Both filtrate and washings were caught in a weighed 100 cc. beaker. The solvent was evaporated and the beaker dried at 100 degrees C., cooled in a vacuum dessicator, and weighed.

Calculations. Weight of residue x 200 = gms. of fat in total sample.

Table I

Calcium and magnesium values in blood serum and urine for K.R., a young female student.

A. Without medication.

Date	Calcium		Magnesium	
	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
2/20/41	9.91	0.204	1.90	0.102
2/21/41	9.81	0.205	2.07	0.073
2/22/41	9.94	0.222	2.25	0.096
2/24/41	10.30	0.340	2.30	0.108
2/25/41	11.00	0.292	1.80	0.113
3/31/41	10.30		2.50	
4/1/41	9.50	0.260	2.27	0.132
Total	70.76	1.523	14.09	0.626
Average	10.11	0.253	2.13	0.104

B. 6 gms. of magnesium trisilicate per day, started 4/1/41.

4/2/41*	10.18	0.292	4.50	0.100
4/3/41	10.70		1.80	
4/4/41	10.37	0.370	1.91	0.188
4/5/41	10.46	0.326	1.80	0.200
Total	41.71	0.988	9.81	0.488
Average	10.43	0.329	2.45	0.165

*She was very drowsy and noticed slight diarrhea. Drowsiness continued throughout the experiment.

The urine specimen for 4/3/41 was accidentally lost.

Table II

Calcium and magnesium values in blood serum and urine for B.D. a female medical student.

A. Without medication.

Date	Calcium		Magnesium	
	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
2/21/41	11.2	0.181	1.71	0.055
2/23/41	11.3	0.208	2.30	0.058
2/24/41	12.0	0.273	2.00	0.097
2/25/41	10.4	0.187	1.67	0.058
2/26/41	11.9	0.240	2.12	0.087
4/2/41	10.27	———	1.80	———
Total	67.07	1.089	11.60	0.355
Average	11.18	0.218	1.93	0.071

B. 6 gms. of magnesium trisilicate per day, started 4/2/41

4/3/41	10.28	0.199	1.80	0.343
4/4/41	9.99	0.252	1.90	0.101
4/5/41	10.38	0.216	1.80	0.144
4/6/41	10.19	0.272	2.06	0.183
4/7/41	10.48	0.304	2.15	0.098
Total	51.32	1.243	9.71	0.869
Average	10.27	0.248	1.94	0.174

No unusual symptoms were noted throughout the experiment.

Table III

Calcium and magnesium values in blood serum and urine for R.H., a male medical student.

A. Without medication.

Date	Calcium				Magnesium	
	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
4/15/41	10.90				2.08	
4/16/41	10.65	0.250	6.45	23.90	2.24	0.075
4/17/41	11.13	0.230	5.70	40.28	1.90	0.070
4/18/41	11.15	0.240	5.70	35.09	2.20	0.114
4/19/41	11.25	0.277	6.00	34.08	1.72	0.119
4/21/41	10.83	———	———	———	2.35	———
Total	65.91	0.997	23.85	133.35	12.49	0.378
Average	10.98	0.249	5.96	33.34	2.08	0.094

B. 6 gms. of magnesium trisilicate per day, started 4/21/41.

4/22/41	10.57	0.292	6.90	28.00	1.07	0.090
4/23/41	10.35	0.324	6.35	20.40	2.00	0.156
4/24/41	10.76	0.208	6.80	26.79	2.40	0.215
4/25/41	10.73	0.214	6.00	16.37	1.72	0.097
4/26/41	10.54	0.200	6.00	29.40	2.07	0.081
Total	52.95	1.139	31.75	122.96	9.26	0.629
Average	10.59	0.228	6.35	24.59	1.85	0.126

Only a slight sleepiness was noted which lasted throughout the experiment.

Table IV

Calcium and magnesium values in blood serum and urine for C.W., a male medical student.

A. Without medication.

Date	Calcium				Magnesium	
	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
4/5/41	10.48				2.50	
4/6/41	10.48				1.55	
4/7/41	10.45	0.408	5.50	49.22	1.95	0.122
4/8/41	10.54	0.350	5.90	34.24	1.95	0.112
4/9/41	9.89	0.418	6.50	31.20	1.63	0.126
4/10/41		0.440	5.90	39.60		0.100
4/12/41	9.98	0.376	5.50	59.40	2.17	0.108
Total	61.82	1.994	29.30	213.66	11.75	0.568
Average	10.30	0.399	5.86	42.73	1.96	0.114

B. 6 gms. of magnesium trisilicate per day, started 4/12/41. He was very nauseated after taking 4 gms.

4/13/41	9.88	0.306	6.00	37.26	2.60	0.093
4/14/41	9.70	0.264	5.80	36.00	2.40	0.086
4/15/41	9.50	0.360	5.90	33.25	1.70	0.106
4/16/41	10.27	0.380	5.80	39.20	1.72	0.093
4/17/41	10.27	0.430	6.20	37.10	2.25	0.117
Total	49.62	1.740	29.70	182.81	10.67	0.495

Table IV continued.

	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
Average	9.92	0.348	5.94	36.56	2.13	0.099

Except for the nausea noted on the first day of medication, there were no other symptoms.

Table V

Calcium and magnesium values in blood serum and urine for E.B.W., a male professor.

A. Without medication.

Date	Calcium		Magnesium	
	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
2/20/41*	10.30	0.368	1.73	0.109
2/21/41	10.50	0.462	1.99	0.143
2/22/41	11.70	0.320	2.36	0.073
2/24/41	10.20	0.330	2.25	0.093
2/25/41	11.70	0.332	2.10	0.090
2/27/41	11.30	0.305	2.04	0.084
2/28/41	11.00	———	2.59	———
Total	76.70	2.117	15.06	0.592
Average	10.96	0.353	2.15	0.099

* Calcium acid phosphate was taken on this date, and was excreted in the urine on the following day.

B. 6 gms. of magnesium trisilicate per day, started 2/28/41

3/1/41	11.00	0.375	5.24	0.178
3/2/41	10.80	0.333	2.88	0.152
3/3/41	10.50	0.366	2.07	0.247
3/4/41	10.10	0.252	1.80	0.104
3/5/41	9.90	0.280	2.00	0.140

Table V continued.

Date	Calcium Serum mgms. per 100 cc.	Calcium Urine gms. per 24 hrs.	Magnesium Serum mgms. per 100 cc.	Magnesium Urine gms. per 24 hrs.
3/6/41	11.10	0.238	2.04	0.094
Total	65.20	1.864	16.03	0.915
Average	10.53	0.307	2.67	0.152

He noticed a drowsiness on 3/1/41, which increased over a period of about 4 days, and then gradually went away.

C. E.C.W. was continuing to take 6 gms. of trisilicate per day.

3/19/41	9.00	0.300	2.36	0.160
3/20/41	10.90	0.356	2.00	0.160
3/21/41	11.00	0.320	2.35	0.173
Total	30.90	0.976	6.71	0.493
Average	10.30	0.325	2.34	0.164

About 4/1/41 he began to notice a marked regularity of bowels, and a rather disagreeable taste in his mouth.

D. The same trisilicate routine was being continued.

Date	Calcium Serum mgms. per 100 cc.	Calcium Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Magnesium Serum mgms. per 100 cc.	Magnesium Urine gms. per 24 hrs.
4/14/41	10.35	0.404	6.15	43.13	2.52	0.159
4/15/41	10.35	09348	5.40	38.54	2.17	0.153

Table V continued

E. The same trisilicate routine continued.

Date	Calcium				Magnesium	
	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
4/21/41 *	10.74	0.419	5.90	34.06	2.08	0.206
4/22/41	10.48	0.280	5.55	40.65	2.37	0.126
4/23/41	10.49	0.110	5.00	48.88	2.70	0.334
4/24/41	10.18	0.206	5.00	50.50	1.25	0.248
Total	41.89	1.017	21.45	174.09	8.40	0.914
Average	10.47	0.254	5.36	43.52	2.10	0.229

* On this date K.S.W. began to have severe diarrhea and therefore stopped taking magnesium trisilicate. The diarrhea continued throughout the dates in the table and gradually decreased

Table VI

Calcium and magnesium values in blood serum and urine for S.T., a professor.

A. Without medication.

Date	Calcium				Magnesium	
	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
6/18/41	10.79				2.00	
6/19/41	10.79	0.081	5.50	39.74	2.12	0.061
6/20/41	10.79	0.104	5.10	65.82	2.20	0.076
6/21/41		0.160	5.20	81.90		0.042
6/23/41	10.64	0.187	4.75	53.20	2.28	0.083
6/24/41	10.67	0.308	5.20	55.75	2.28	0.064
Total	53.83	0.840	25.75	294.41	10.88	0.346
Average	10.76	0.168	5.15	58.88	2.18	0.069

B. 6 gms. of magnesium trisilicate per day, started 6/24/41.

6/25/41	10.67	0.238	5.20	66.99	2.15	0.096
6/26/41	10.89	0.254	5.25	71.90	2.50	0.114
6/27/41	10.67	0.220	5.30	79.20	2.50	0.175
6/28/41	10.48	0.188	5.30	90.00	2.13	0.170
Total	41.91	0.900	21.05	298.09	9.28	0.555
Average	10.48	0.225	5.26	74.52	2.32	0.139

Table VI continued.

C. The tricilicate routine continued, and 3 doses of hydrochloric acid, each equivalent to 54.80 cc of N/10 acid, taken daily before meals, was started 6/26/41.

	Calcium				Magnesium	
Date	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
6/29/41	10.09	0.280	5.00	110.00	1.93	0.225
6/30/41	10.77	0.261	5.00	114.00	2.03	0.202
Total	20.86	0.541	10.00	224.00	3.96	0.427
Average	10.43	0.270	5.00	112.00	1.98	0.214

There were no unusual symptoms noted throughout the entire experiment.

Table VII

Calcium and magnesium values in blood serum and urine for P.S., a diagnosed peptic ulcer case.

A. On a peptic ulcer diet, but without medication.

	Calcium				Magnesium	
Date	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
6/18/41	10.69				1.90	
6/19/41	10.69	0.508	5.60	57.75	1.90	0.145
6/20/41	10.69	0.416	6.00	51.00	1.95	0.114
6/21/41		0.420	6.40	54.10		0.123
6/23/41	10.67	———	———	———	1.99	———
Total	42.74	1.344	18.00	162.85	7.74	0.380
Average	10.69	0.446	6.00	54.28	1.94	0.127

B. 6 gms. of magnesium trisilicate, started 6/23/41

6/24/41	11.15	0.300	6.70	18.60	1.99	0.124
6/25/41	11.15	0.426	6.45	68.60	1.95	0.198
6/26/41	10.67	0.476	6.75	54.00	2.27	0.270
6/27/41	11.05	0.300	6.75	21.60	2.23	0.213
Total	44.02	1.502	26.65	162.80	8.44	0.805
Average	11.00	0.376	6.66	40.70	2.11	0.201

No unusual symptoms were noted throughout the entire experiment.

Table VIII

Calcium and magnesium values in blood serum and urine for E.S.W., three months after discontinuing magnesium trisilicate.

A. Without medication.

	Calcium				Magnesium	
Date	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
7/21/41	11.10	0.224	5.70	51.94	1.55	0.060
7/22/41	11.33	0.228	6.50	51.52	1.55	0.060
Total	22.43	0.452	12.20	103.46	3.10	0.120
Average	11.22	0.226	6.10	52.73	1.55	0.060

B. 6 gms. of magnesium trisilicate, started 7/22/41.

7/23/41	11.09	0.492	6.35	52.80	1.22	0.050
7/24/41	11.09	0.400	7.11	12.88	2.22	0.087
7/25/41	11.48	0.358	5.70	31.00	1.38	0.129
7/26/41	11.39	0.326	6.30	23.92	1.63	0.093
7/27/41	11.39	0.401	6.30	55.21	1.29	0.068
7/28/41*	11.38	0.340	5.60	48.00	1.40	0.044
7/29/41	11.08	0.224	6.00	54.39	1.30	0.040
Total	78.90	2.541	43.35	278.20	10.64	0.511
Average	11.27	0.363	6.19	39.74	1.52	0.073

* Stopped trisilicate on this date.

Drowsiness was noted for several days after beginning trisilicate. Diarrhea continued throughout the medication period.

Table IX

Calcium and magnesium values in blood serum and urine for M.C., a diagnosed peptic ulcer case.

This man had been taking magnesium trisilicate for several months. One week previous to this experiment he began to take 6 gms. per day, and continued on this routine throughout the dates in this table.

	Calcium				Magnesium	
Date	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.	pH of Urine	Titrable acidity	Serum mgms. per 100 cc.	Urine gms. per 24 hrs.
6/23/41	11.45	0.181	6.00	41.07	2.15	0.204
6/24/41	10.67	0.306	5.60	38.77	2.20	0.183
6/25/41	11.02	0.274	6.00	46.21	1.65	0.152
6/26/41	11.06	0.250	6.00	42.80	1.90	0.140
Total	44.19	1.011	23.60	168.85	7.85	0.654
Average	11.05	0.253	5.90	42.21	1.96	0.164

Table X

Calcium and Magnesium values in blood serum for E.S.W.

A. Without medication.

Time	8/11/41	Serum Calcium	Serum Magnesium
8:00 AM		10.04 mgms. %	1.67 mgms. %

B. 6 gms. of magnesium trisilicate taken at 8:10 AM.

8:40 AM	10.04 mgms. %	1.75 " %
9:10 AM	10.04 " "	2.30 " "
9:40 AM	10.23 " "	2.30 " "
10:10 AM	10.04 " "	2.43 " "
11:00 AM	10.42 " "	2.43 " "
12:00 AM *	10.23 " "	2.52 " "
2:00 PM	10.42 " "	3.63 " "
4:00 PM	10.23 " "	2.43 " "
Average	10.20 " "	2.47 " "

C. 24 hrs. after taking trisilicate.

8:10 AM	10.34 "	2.59 "

* Drowsiness became noticible at this time. It was marked at 2:00 Pm and had decreased by 4:00 PM.

Table XI

Calcium and Magnesium values
in blood serum for E.S.W.

A. 24 hrs. after ingestion of 6 gms. of magnesium trisilicate.

Time	8/12/41	Serum Calcium	Serum Magnesium
8:10		10.34 mgms. %	3.55 mgms. %

B. 6 gms. of trisilicate were taken at 8:10 AM. A total of 75 cc. of N/10 HCl were taken in 3 doses of 25 cc. each at 8:10, 9:10, and 10:10 AM.

9:10 AM		10.34 mgms. %	2.46 mgms. %
10:10 AM		10.34 " "	2.46 " "
12:00 AM		10.42 " "	2.80 " "
2:00 PM *		10.42 " "	4.67 " "
4:00 PM		10.43 " "	2.09 " "
Average		10.39 " "	2.94 " "

* Decided drowsiness was noted at this time.

C. 24 hrs. after 6 gms. of trisilicate, taken 8/12/41.

8:10 AM	8/13/41	10.42 " "	2.63 " "

Table XII

Effect of Trisilicate upon food utilization and feces and urine acidity for E.S.W.

A. Without medication.

Date	Gms. Total Nitrogen Feces	Urine	U.N./F.N.	Gms. Fat Feces	Gms. Carbohydrate fermentable Feces	pH Urine	Feces	Titrable acidity Urine
7/14/41	0.480			9.20	0.27		6.35	
7/15/41	1.600	11.50	7.2	6.00	0.53	5.10	6.35	59.20
7/16/41	0.768	15.26	20.0	5.00	0.37	5.15	6.95	64.68
7/17/41	1.280	17.60	12.7	1.00	0.71*	5.20	6.90	54.91
7/18/41	0.800	16.40	20.5	7.00		5.05	5.60	54.45
7/19/41	0.920	18.33	20.0	4.30		5.25	5.90	61.10
7/20/41		16.12				5.70		51.52
7/21/41	2.120	16.72	7.8	2.00	____	6.50	6.50	51.94
Total	8.063	111.94	88.2	34.50	1.88	38.05	44.50	397.80
Average	1.152	15.99	14.7	4.93	0.47	5.44	6.36	56.83

* This group of normal carbohydrates was determined 7/29/41 to 8/1/41

Table XII continued.

B. 6 gms. magnesium trisilicate, started 7/22/41

Date	Gms. Total Nitrogen Feces	Urine	U.N./F.N.	Gms. Fat Feces	Gms. Carbohydrate fermentable Feces	pH Urine	Feces	Titrable acidity Urine
7/23/41	2.96	22.28	7.5	2.00		6.35	5.35	52.80
7/24/41	1.08	20.60	19.1	4.00	0.04	7.11	7.40	12.88
7/25/41	2.08	18.60	9.0	2.80	0.18	5.70	6.25	31.00
7/26/41	1.92	18.30	9.5	4.40	0.86	6.30	7.10	23.92
7/27/41	2.68	16.88	6.3	4.60	0.21	5.60	7.10	35.21
7/28/41	2.44	24.00	9.8	6.80	0.37	6.00	7.20	48.00
Total	13.16	120.66	81.2	24.60	1.66	37.06	40.40	223.81
Average	2.19	20.11	10.2	4.10	0.33	6.18	6.73	37.30

No unusual symptoms were noted throughout this period.

Table XII continued.

C. Trisilicate was discontinued 7/28/41

Date	Gms. Total Nitrogen			Gms. Fat	Gms. Carbohydrate fermentable	pH		Titrable acidity
	Feces	Urine	U.N./F.N.	Feces	Feces	Urine	Feces	Urine
7/29/41	2.14	18.32	8.5			5.30	6.80	54.39
7/30/41	2.36	17.92	7.6			6.10	6.90	40.00
7/31/41	2.08	19.60	8.5			5.10	6.80	58.86
8/1/41	2.40	18.01	7.5			4.75	6.20	48.38
8/2/41	1.80	18.85	10.5			5.30	6.65	44.63
8/3/41	1.24	12.40	10.0		0.71	5.40	5.60	45.10
8/4/41	2.64	13.20	5.0		0.42	5.90	6.55	39.00
8/5/41	1.80	17.80	9.9		0.45	5.55	7.05	57.10
8/6/41	1.80	15.50	8.6		0.36	5.35	5.20	31.98
8/7/41	1.80	16.36	9.9		0.19	5.20	5.90	32.80
Total	20.06	167.96	86.0		2.13	53.95	63.56	452.38
Average	2.06	16.80	8.6		0.43	5.40	6.35	45.24

Table XIII

Effect of trisilicate upon food utilization and feces and urine acidity for C.P.

A. Without medication.

	Gms Total Nitrogen			Gms. Fat	Gms. Carbohydrate fermentable	pH		Titrable acidity
Date	Feces	Urine	U.N. / F.N.	Feces	Feces	Urine	Feces	Urine
7/12/41	1.60	11.11	6.94	12.00	0.600 *	6.00		45.60
7/13/41	0.76	8.56	11.30	2.60	0.540	6.00		27.60
7/14/41	0.48	10.98	22.90	2.00	0.484	6.00	6.55	9.40
7/15/41	0.80	8.24	10.30	2.00	0.550	6.80	7.60	12.32
7/16/41	0.48	7.68	16.00	2.40		6.15	6.30	20.00
7/17/41	0.96	6.85	7.10	1.00		5.25	6.80	28.35
7/18/41	1.48	8.51	8.00	8.40		5.15	6.15	33.30
7/19/41	0.68	5.40	8.00	0.72		5.25	5.25	8.30
7/20/41	0.68	11.30	18.70	2.12			6.20	28.00
Total	8.12	78.33	101.24	33.24	2.374	46.30	44.85	201.48
Average	0.90	8.70	11.25	3.70	0.575	5.83	6.41	22.38

*This group of carbohydrate values was determined 8/2/41 to 8/5/41.

Table XIII continued

B. 6 gms. of magnesium trisilicate per day, started 7/20/41

Date	Gms. Total Nitrogen			Gms. Fat	Gms. Carbohydrate fermentable	pH		Titrable acidity
	Feces	Urine	U.N./F.C.	Feces	Feces	Urine	Feces	Urine
7/21/41*	1.40	6.38	4.8	4.40		6.80	7.10	12.00
7/22/41	2.52	7.90	3.1	8.40		5.60	6.80	9.30
7/23/41	1.64	6.05	4.2	2.00		7.10	7.60	4.80
7/24/41	2.08	8.64	4.0	2.60	0.34	5.75	8.15	10.22
7/25/41	1.60	7.02	4.4	7.40	0.08	6.40	6.25	10.40
7/26/41	2.30	7.92	3.4	2.00	0.30	7.10	8.00	5.76
7/27/41	5.00	7.77	2.6	4.40	0.50	6.60	6.00	12.34
Total	16.54	54.19	28.0	31.20	1.22	44.85	52.31	64.92
Average	2.08	7.74	4.0	4.46	0.31	6.41	8.47	9.27

* Marked diarrhea occurred during the following four days, and then gradually disappeared. No other symptoms were noted.

Table XIII Continued.

C. One week after magnesium trisilicate was discontinued.

Date	Gms. Total Nitrogen Feces	Urine	U.N./F.N.	Gms. Fat Feces	Gms. Carbohydrate fermentable Feces	pH Urine	Feces	Titrable acidity Urine
8/2/41	1.60	13.40	9.62			6.00	6.00	14.00
8/3/41	1.40	12.40	9.00			6.00	6.00	12.34
8/4/41	0.80	10.00	12.25			6.15	6.85	13.25
8/5/41	1.00	10.40	10.50			6.70	7.00	17.03
Average	1.20	12.05	10.34			6.21	6.61	14.16

The subject of this experiment showed a low titrable acidity. A gastric analysis was done with the following results:

	N/10 HCl	N/10 Total acid.
Residuum	4 cc.	10 cc.
30 min. after gastric meal*	2 cc.	20 cc.
Histamine**		
15 min. after injection	20 cc.	38 cc.

Table XIII continued.

30 min. after injection	28 cc.	40 cc.
45 min. " "	24 cc.	40 cc.
60 min. " "	20 cc.	22 cc.

* The gastric meal consisted of 2 crackers and 1 glass of water.

** 0.25 cc of 1-1000 solution of histamine, given subcutaneously.

In order that the effect of trisilicate ingestion may be seem more clearly the tables below show the average values for the experimental periods for each individual and the averages of these individual averages.

Table XIV

	Serum Calcium		Urine Calcium	
	Normals	Medication	Normals	Medication.
K.R.	10.11	10.42	0.254	0.329
B.D.	11.18	10.07	0.218	0.248
R.R.	10.98	10.59	0.249	0.228
C.W.	10.30	9.92	0.399	0.348
E.W.	10.96	10.58	0.353	0.307
W.T.	10.78	10.48	0.168	0.125
P.S.	10.69	11.09	0.446	0.376
Average	10.72	10.45	0.298	0.294

Percentage decrease = 2.7% Percentage decrease = 1.3%

	Serum Magnesium		Urine Magnesium	
K.R.	2.13	2.45	0.104	0.163
B.D.	1.93	1.94	0.071	0.174
R.R.	2.08	1.86	0.094	0.126
C.W.	1.96	2.13	0.114	0.099
E.W.	2.15	2.34	0.099	0.153
W.T.	2.18	2.32	0.069	0.139
P.S.	1.94	2.11	0.127	0.201
Average	2.05	2.16	0.097	0.151

Percentage increase = 5.3% Percentage increase = 55.6%

Table XIV continued.

	pH		Titrable Acidity	
	Normals	Medication	Normals	Medication
R.R.	5.96	6.35	33.34	24.69
C.W.	5.86	5.94	42.73	36.56
E.W.	5.61	6.18	59.52	54.39
W.T.	5.15	5.26	58.68	74.52
P.S.	6.00	6.66	54.28	40.70
C.P.	5.97	6.41	22.38	9.27
Average	5.74	6.12	45.19	40.00

Percentage increase = 6.6%. Percentage decrease = 11.5%.

DISCUSSION

In this study of magnesium trisilicate in the body, there seemed to be little effect upon the serum calcium. In the case of some individuals it increased slightly after trisilicate ingestion and in others it decreased similarly, as an average decreased 2.7 per cent. The same situation was noted for the urine calcium, the per centage decrease being 1.3 In the experiment carried out over a period of seven weeks there was a slight increase in urinary output of calcium at the end of the experiment. When medication was stopped the calcium output decreased markedly.

In most cases the effect of trisilicate on the fasting serum magnesium was to increase it slightly, the average increase being 5.3 per cent. Only two individuals out of seven showed any marked increase, this occurring at the end of twenty-four hours.

The magnesium curves run on E.S.F. brought out the interesting fact that regardless of the acidity of the gastro-intestinal tract maximum absorption of a dose of six gms. of trisilicate occurs in six hours. At the six hour period the greatest sedative action was noted. The ingestion of 75 cc. of N/10 hydrochloric acid markedly increased the absorption of magnesium. The maximum serum magnesium with trisilicate and hydrochloric acid was 34 per cent higher than with trisilicate alone.

The effect of trisilicate on the urinary excretion of magnesium was extremely marked. The average increase was 55.6 per cent, and in

one case, B.D., the amount excreted was more than doubled.

The urinary pH was increased in every case by trisilicate ingestion, the average increase being 6.6 per cent. Correspondingly the titrable acidity decreased in every case except one, the average lowering being 11.5 per cent. Fecal pH was increased an average of 11 per cent.

In the digestion-absorption experiments performed on two subjects, the results were more striking in one case than in the other, but both showed definite changes. There was on an average 107 per cent increase on fecal nitrogen after medication. The sum of urinary and fecal nitrogen for C.P. during the normal period was 9.60 gms. and during the trisilicate routine was 9.82 gms. On the other hand the sum in the case of E.S.W. was 17.14 gms. during the control period and 22.30 gms. during the experimental period. The weather was unusually warm during the control period which might account for the decreased ingestion of protein by E.S.W. The ratio of urinary nitrogen to fecal nitrogen decreased 46 per cent during the experimental period.

There are three possible ways in which magnesium trisilicate may cause increase in fecal nitrogen:

1. The magnesium trisilicate may adsorb and inactivate proteolytic enzymes.

2. Deposition of trisilicate on the intestinal epithelium may occur with a decrease in permeability to protein digestion products.

3. Trisilicate may interfere with peptic digestion of

protein in the stomach as the result of neutralization of gastric juice.

There was essentially no effect on fat absorption. The average amount of fat found in the stool per twenty-four hours during the control period was 4.38 gms. and during the trisilicate routine was 4.28 gms.

Carbohydrate absorption was likewise unaffected. The average fermentable carbohydrate after acid hydrolysis, calculated as glucose per twenty-four hour stool in the control period was 0.55 gms. and in the trisilicate period was 0.32 gms. These results show better than 99 per cent efficiency of utilization in both control and experimental periods.

CONCLUSIONS

Six grams of magnesium trisilicate, taken three times daily in doses of two grams each, resulted in the following:

1. No appreciable effect upon serum calcium.

2. No immediate effect on urinary calcium output, but an increase in the latter after several weeks of continuous medication.

3. A slight increase in serum magnesium in most cases, with a marked effect in a few cases.

4. A marked increase in urinary output of magnesium, almost doubled in most cases.

5. An appreciable increase in the pH of both urine and feces.

6. A decrease in urinary titrable acidity.

7. An interference with protein absorption as indicated by a marked increase in fecal nitrogen and a decrease in the urinary to fecal nitrogen ratio.

8. No appreciable effect on fat absorption.

9. No appreciable effect on carbohydrate absorption.

A single dose of six grams of trisilicate resulted in the following:

1. No effect on serum calcium.

2. Increased serum magnesium with a maximum value in six hours.

The addition of hydrochloric acid to the trisilicate routine resulted in the following:

1. A rise in serum magnesium.

2. No effect on serum calcium.

3. An increase in urinary calcium.

4. An increase in urinary magnesium.

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