Bio-availability of calcium and magnesium from magnesium citrate calcium malate

Implications for osteoporosis prevention

Johan B Ubbink, W J Hayward Vermaak, Rhena Delport, Annatjie van der Merwe

Objectives. To assess the bio-availability of calcium and magnesium from an organic complex (magnesium citrate calcium malate (MCCM)) and to characterise MCCM supplementation with regard to the parathyroid hormone (PTH) response, acid-base homeostasis and selective parameters of bone resorption and formation.

Design. Controlled trial where oral MCCM and water were compared. Administration of citrate and malate with potassium and sodium as counter cations served as control treatment.

Subjects. Sixteen apparently healthy women.

Setting. Institute of Pathology, University of Pretoria.

Outcome measures. Plasma ionised calcium, serum intact PTH, serum osteocalcin, urine calcium, magnesium and deoxypyridinoline and blood bicarbonate, as well as blood and urine pH, were monitored in the study.

Results. Compared with water, a single oral dose of 5 g MCCM (containing 500 mg calcium and 250 mg magnesium) resulted in significant increases in plasma ionised calcium (3.1%; P < 0.01), urine calcium (213.6%; P < 0.001), urine magnesium (212.6%; P < 0.001) and blood standard bicarbonate (3.8%; P < 0.05) concentrations, while serum intact PTH concentrations decreased (-31.6%; P < 0.001). Citrate and malate per se had no calcicuric effect. Following 12 - 13 days of MCCM treatment, the mean (SD) urinary deoxypyridinoline excretion declined from 8.01 (3.02) to 6.95 (2.39) nmol/mmol creatinine (P = 0.012).

Conclusions. MCCM is a suitable compound for both calcium and magnesium delivery. Treatment with MCCM may result in reduced bone resorption, as indicated by lower intact serum PTH concentrations and less urinary deoxypyridinoline excretion.

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An adequate calcium intake is recommended as a potential prophylactic measure against osteoporosis. Postmenopausal women with a typical dietary calcium intake of about 700 mg/day have been reported to have a net intestinal calcium absorption efficiency of about 10%, and a calcium intake of approximately 1 200 mg per day is required to approach positive calcium balance. Since few women consume a diet sufficiently rich in calcium, they often depend on calcium supplements to ensure an adequate daily intake.

Calcium balance may also be achieved on lower calcium intakes if the obligatory calcium losses from the body can be limited. It is not always appreciated that the skeleton serves as a substantial reservoir of labile base in the form of the alkaline salts of calcium; these are mobilised to maintain plasma bicarbonate concentrations and blood pH during an acid load. For example, a diet-modulated increase in the rate of endogenous acid production has been shown to reduce blood pH and bicarbonate concentrations significantly in healthy subjects. A lower pH and plasma bicarbonate concentration is a strong and independent signal for the stimulation of bone resorption and inhibition of bone formation. Eventually, the calcium reabsorbed from bone is lost in the urine, thus contributing to a negative calcium balance and a higher dietary calcium requirement to restore calcium balance.

It has been shown recently that the acidifying effect of a high-protein diet may be neutralised by daily oral administration of potassium bicarbonate. This resulted in a lower rate of urinary calcium excretion, reduced bone resorption and an increased rate of bone formation. A calcium salt with a systemic alkalinising effect may therefore be the supplement of choice in strategies to prevent osteoporosis.

A second mechanism to optimise calcium supplementation may be the addition of magnesium to the supplement. Magnesium deficiencies were already implicated in 1960 in the pathogenesis of osteoporosis. It is known that magnesium depletion may impair calcium homeostasis as reflected in hypocalcaemia, impaired parathyroid hormone (PTH) secretion and low circulating concentrations of 1,25 dihydroxyvitamin D. The effect of a magnesium deficiency is explained by observations that PTH release from the parathyroid gland is magnesium-dependent, while end-organ resistance towards PTH has also been described during magnesium deficiency. Despite the well-described dependency of calcium metabolism and homeostasis on an adequate magnesium status, there is a perception that magnesium and calcium should not be supplemented concomitantly. This perception is presumably based on earlier studies performed in rats which showed competition between magnesium and calcium uptake from the gastro-intestinal tract. In humans, however, a high dietary magnesium intake does not affect calcium absorption. Given that many individuals consume less magnesium than the recommended daily allowance (RDA), it makes sense to supplement calcium and magnesium together, provided that both minerals are presented in a bio-available form.

This study investigates the characteristics of calcium supplementation in the form of a magnesium-containing salt with an alkalinising metabolic effect (magnesium citrate...
Materials and methods

Study design. The study was designed as a controlled trial where selective metabolic effects of a single 5 g dose of MCCM (composition: 500 mg elemental calcium, 250 mg elemental magnesium, 2.06 g citrate, 1.41 g malate, supplied as OsteoMatrix-CM by Vesta Medicines, Johannesburg) were compared with those of placebo (distilled water). Citrate and malate with potassium and sodium as counter cations (citrate/malate control (CMC): 2.30 g KHCO₃, 1.94 NaHCO₃, 2.06 g citric acid, 1.41 g malic acid) were used as a control.

Subjects. The study was approved by the Human Ethics Committee of the University of Pretoria. Blood samples were obtained from adult women volunteers aged over 21 years, who did not use any calcium or magnesium supplements for 3 months prior to study entry. Inclusion criteria were: (i) a serum creatinine concentration < 140 μmol/l; (ii) a blood platelet count > 150 × 10⁹/l; (iii) serum gamma-glutamyl transferase, alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase activities of < 46 IU/l, < 35 IU/l, < 35 IU/l and < 110 IU/l, respectively; (iv) a serum total calcium concentration between 2.20 and 2.55 μmol/l; and (v) a serum intact PTH (iPTH) concentration between 10 and 65 ng/l.

Prospective participants with a history of peptic ulcer, intestinal resection, regional enteritis, malabsorption, bone disease, diabetes or alcohol/drug abuse were excluded. Prospective participants were also excluded if they reported treatment with vitamin K antagonists, intravenous heparin, calcium channel blockers, vitamin D or vitamin D derivatives 3 months prior to study entry.

Volunteers who fulfilled the criteria as outlined above gave informed consent before they were allowed to enter the study. Eight pre- and 8 postmenopausal women were enrolled in the trial and were requested to visit the laboratory consulting rooms four times. For 2 days prior to the first visit, the participants followed a diet restricted in calcium (400 mg/day). From 20h00 on the day preceding visit 1, the participant started to fast, except for 500 ml distilled water which was consumed at 20h00 and again at 23h00. On the morning of the second day, the participants were randomised into two groups, groups A (N = 8) and B (N = 8). At 07h00 on the test day, the patient voided and urine was collected between 07h00 and 09h00 (sample 1). At 09h00 the participants from group A drank a further 300 ml distilled water, while participants from group B took an oral dose of CMC dissolved in 300 ml distilled water. At 09h00 and 11h00, the participants received a further 400 ml and 300 ml distilled water, respectively. Urine was collected between 09h00 and 11h00 (sample 2) and between 11h00 and 13h00 (sample 3). Blood samples in clotting tubes, in tubes with EDTA as anticoagulant and in heparinised syringes were obtained directly before administration of water at 09h00, as well as 1 and 4 hours later.

One week later, the abovementioned study protocol was repeated, except that on the morning of the test day, group A consumed CMC dissolved in water as described above, while group B drank only water.

Another week later, the abovementioned study protocol was repeated, except that 5 g MCCM, dissolved in 300 ml distilled water, was administered. Subsequently, each participant received a box containing 30 sealed sachets. Each sachet contained 2.5 g MCCM. They were requested to take the contents of one sachet, dissolved in a glass of water, in the morning and one sachet in the evening. Participants were requested to return the unused sachets at the last visit (visit 4).

Visit 4 took place after the participants had been treated with MCCM for 2 weeks. On the day preceding visit 4, participants collected a 2-hour (between 07h00 and 09h00) urine sample. The last MCCM dose was taken on the morning of the day preceding the day of visit 4. The study protocol as described for visit 1 was then repeated, except that the participants were not required to consume a low-calcium diet in the 2 days preceding visit 3. The returned sachets were counted and the mean daily mass of MCCM used per participant was calculated and recorded.

Laboratory investigations. The heparinised blood samples were kept on ice and analysed for pH and blood gases (ABL 3 analyser, Radiometer, Copenhagen) within 20 minutes after the sample had been obtained. Ionised calcium concentrations were determined (ICA2, Radiometer, Copenhagen) and adjusted for plasma pH. The remainder of the heparinised blood samples were transferred to glass centrifuge tubes and the blood cells were removed by low-speed centrifugation. The plasma obtained was used for total calcium, magnesium and albumin determination (Technicon Dax 48, Miles Inc., Tarrytown, NY, USA); calcium concentrations were adjusted for albumin concentrations. Serum samples were stored at −70°C for analysis at a later stage. Serum iPTH was analysed by means of a two-site immunoradiometric assay (IRMa) obtained from Nichols Institute Diagnostics (San Juan Capistrano, CA 92675, USA). Fasting serum osteocalcin concentrations were measured by radio-immunoassay (INSCAR Co., Stillwater, MN, USA).

The volume and pH of each urine sample was recorded. Subsequently, two 30 ml volumes of urine were stored at −70°C and the remainder of each urine sample was acidified to a pH < 1.0 by the addition of concentrated (35%) HCl solution. Two 0.01 ml aliquots of acidified urine samples were stored at −70°C for analysis of urinary calcium and magnesium concentrations. The latter element concentrations were determined in duplicate with a PerkinElmer model 3030 atomic absorption spectrophotometer. Urinary creatinine concentrations were determined in duplicate with an Astra 8 Routine Analyser from Beckman Instruments (Irvine, Calif., USA). Duplicate determinations were done in different batches and on different days.

Urinary deoxypyridinoline (Dpd) concentrations were determined by means of competitive enzyme-linked immunosassay (Pyrilinks-D, Metra Biosystems, Mountain View, Calif., USA). Only the first urine samples (obtained between 07h00 and 09h00) were analysed and the samples obtained at visits 1 to 3 were considered as baseline samples, i.e. prior to any calcium supplementation. Samples obtained the day before visit 4 and at visit 4 were considered to reflect the effect of short-term calcium supplementation of Dpd excretion. Urinary Dpd excretion was expressed as nmol Dpd/mmol creatinine.
Statistical analyses. Observed data generally showed normal distributions and parametric statistics were used. Unless otherwise indicated, the effects of the various treatments were compared with the effect of water consumption by using the paired t-test. Urinary Dpd excretion showed a non-parametric distribution and Wilcoxon's matched-pairs signed ranks test was used to evaluate the effect of calcium supplementation on this parameter of bone resorption.

Results
Fifteen participants completed the study successfully. No side-effects were reported with consumption of MCCM, except in 1 participant who complained of malaise on the morning of visit 4 before the MCCM dose was administered. After administration of MCCM, she vomited and was sent home. Another participant had a normal fasting iPTH concentration during screening, but had consistently elevated fasting iPTH concentrations throughout the study. Data from this latter participant were therefore omitted from the statistical analyses. Results reported here are from 15 participants at visits 1 - 3 and from 14 participants at visit 4. The mean (SD) age of the study population was 37.6 (9.4) years, and the mean body mass was 73.9 (12.7) kg at the start of the study. Between visits 3 and 4, participants consumed 65.2 (1.9) g MCCM, which is equivalent to a compliance rate of 96.5 (2.8)%.

Urinary calcium and magnesium excretion were used as indirect indicators of absorption according to the method described by Harvey et al. Mean urinary calcium and magnesium excretion (expressed as mmol/day at 3 h postdose) were 173.0 (89.7) mmol/day and 126.8 (76.5) mmol/day for MCCM1, respectively. Administration of MCCM had no significant effect on urinary calcium as well as urinary magnesium excretion, but ingestion of the MCCM dose significantly increased urinary excretion of both calcium and magnesium (Table I).

Table I. Urinary calcium and magnesium excretion

<table>
<thead>
<tr>
<th>Visit</th>
<th>Treatment</th>
<th>Calcium excretion (mmol/mmol creatinine)</th>
<th>Magnesium excretion (mmol/mmol creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>-2 - 0 h</td>
<td>0 - 2 h</td>
</tr>
<tr>
<td>1</td>
<td>Water</td>
<td>173.0</td>
<td>124.0</td>
</tr>
<tr>
<td></td>
<td>CMC</td>
<td>126.8</td>
<td>126.0</td>
</tr>
<tr>
<td>2</td>
<td>MCM1</td>
<td>167.2</td>
<td>251.5</td>
</tr>
<tr>
<td></td>
<td>MCM2</td>
<td>150.2</td>
<td>257.7</td>
</tr>
</tbody>
</table>

Results are expressed as mean (SD). CMC = citrate/malate control; MCM1 = first dose of magnesium citrate/calcium malate; MCM2 = second dose of magnesium citrate/calcium malate. The effects of the different treatments were compared with the effect of water consumption by using the paired t-test. The effect of MCM was compared with the effect of MCM1, P < 0.05.

Table II. Plasma ionised calcium, plasma magnesium and serum intact PTH concentrations during treatment

<table>
<thead>
<tr>
<th>Visit</th>
<th>Dose</th>
<th>Plasma ionised calcium (mmol/l)</th>
<th>Plasma magnesium (mmol/l)</th>
<th>iPTH (ng/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Basal 1 h 4 h</td>
<td>Basal 1 h 4 h</td>
<td>Basal 1 h 4 h</td>
</tr>
<tr>
<td>1</td>
<td>Water</td>
<td>1.156 (0.039) 1.161 (0.043) 1.177 (0.052)</td>
<td>0.759 (0.052) 0.743 (0.055) 0.744 (0.056)</td>
<td>34.0 (10.6) 32.3 (10.5) 33.0 (12.2)</td>
</tr>
<tr>
<td></td>
<td>CMC</td>
<td>1.148 (0.049) 1.141 (0.042) 1.163 (0.057)</td>
<td>0.773 (0.046) 0.765 (0.048) 0.749 (0.057)</td>
<td>35.8 (10.2) 40.2 (26.8) 41.6 (19.7)</td>
</tr>
<tr>
<td>2</td>
<td>MCM1</td>
<td>1.163 (0.056) 1.197 (0.049) 1.203 (0.062)</td>
<td>0.781 (0.066) 0.794 (0.068) 0.783 (0.068)</td>
<td>36.0 (16.4) 22.1 (6.9) 27.0 (7.4)</td>
</tr>
<tr>
<td></td>
<td>MCM2</td>
<td>1.151 (0.043) 1.194 (0.035) 1.194 (0.054)</td>
<td>0.768 (0.057) 0.798 (0.057) 0.777 (0.057)</td>
<td>35.4 (15.3) 19.8 (6.9) 24.7 (7.4)</td>
</tr>
</tbody>
</table>

Results are expressed as mean (SD). Plasma ionised calcium concentrations were corrected for pH. The effects of the different treatments were compared with the effect of water consumption: *P < 0.05, **P < 0.01, ***P < 0.001.
Table III. Parameters of acid-base homeostasis during treatment

<table>
<thead>
<tr>
<th>Visit</th>
<th>Treatment</th>
<th>Blood pH</th>
<th>Standard bicarbonate (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Basal 1 h 4 h</td>
<td>Basal 1 h 4 h</td>
</tr>
<tr>
<td>1</td>
<td>Water</td>
<td>7.359 (0.024) 7.362 (0.025) 7.376 (0.030)</td>
<td>23.01 (1.56) 22.99 (1.30) 23.25 (1.64)</td>
</tr>
<tr>
<td>2</td>
<td>CMC</td>
<td>7.346 (0.035) 7.390 (0.036) 7.392 (0.032)</td>
<td>22.38 (1.33) 24.19 (1.38) 23.82 (1.33)</td>
</tr>
<tr>
<td>3</td>
<td>MCCM1</td>
<td>7.361 (0.022) 7.384 (0.022) 7.380 (0.027)</td>
<td>22.60 (1.26) 23.67 (1.16) 23.82 (0.60)</td>
</tr>
<tr>
<td>4</td>
<td>MCCM2</td>
<td>7.356 (0.025) 7.377 (0.028) 7.389 (0.019)</td>
<td>22.94 (1.35) 23.86 (1.31) 23.66 (1.23)</td>
</tr>
</tbody>
</table>

Results are expressed as mean (SD). The paired t-test was used to compare the effect of the different treatments with the effect of water consumption: *0.05 < P < 0.1, **P < 0.05, ***P < 0.01, ****P < 0.001. *indicates significant within-treatment differences when compared with basal concentrations. P < 0.01.

Concentrations were observed 1 hour after administration of MCCM. Four hours later, the mean serum iPTH concentrations were still significantly lower compared with the mean serum iPTH concentration after distilled water consumption (Table II). Small but significant increases were also observed in plasma magnesium concentrations following MCCM administration (Table II).

Table III compares the effect of oral administration of CMC and MCCM on blood pH and standard bicarbonate concentrations. The mean basal standard bicarbonate concentrations, as well as blood pH levels measured prior to administration of either CMC or MCCM, did not differ significantly from those measured when only water was administered. Compared with the consumption of water, the administration of CMC resulted in significant increases in blood standard bicarbonate concentrations (Table III). MCCM consumption also resulted in small increases in standard bicarbonate concentrations which, compared with the effect of water consumption, were only statistically significant in the 1-hour blood sample after the second MCCM dose. However, a within-treatment statistical analysis of the data demonstrated that MCCM consumption significantly raised the standard bicarbonate concentrations from basal levels. The higher bicarbonate concentrations resulted in small but statistically significant increases in blood pH levels after both CMC and MCCM consumption (Table III). Administration of MCCM raised urinary pH significantly; however, the observed increases were less marked than those observed after administration of CMC (Table IV).

Table IV. Urinary pH during treatment

<table>
<thead>
<tr>
<th>Visit</th>
<th>Dose</th>
<th>Urine pH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>-2 - 0 h 0 - 2 h 2 - 4 h</td>
</tr>
<tr>
<td>1</td>
<td>Water</td>
<td>6.53 (0.61) 6.27 (0.55) 6.06 (0.56)</td>
</tr>
<tr>
<td>2</td>
<td>CMC</td>
<td>6.58 (0.61) 7.45 (0.43) 7.16 (0.49)</td>
</tr>
<tr>
<td>3</td>
<td>MCCM1</td>
<td>6.40 (0.57) 6.57 (0.37) 6.13 (0.60)</td>
</tr>
<tr>
<td>4</td>
<td>MCCM2</td>
<td>6.33 (0.57) 6.61 (0.39) 6.27 (0.41)</td>
</tr>
</tbody>
</table>

Results are expressed as mean (SD). The effect of the different treatments were compared with the effect of water consumption: *0.05 < P < 0.1, **P < 0.05, ***P < 0.01, ****P < 0.001, *****P < 0.0001.

Basal urinary Dpd excretion was assessed three times. The 2-hour urine samples (07h00 - 09h00) obtained before the administration of water, CMC and the first MCCM dose were analysed for Dpd and the average value for each individual was considered as basal Dpd excretion. Similar urine samples were obtained the day before visit 4 and at visit 4; the average value of these two collections per individual reflects Dpd excretion during calcium and magnesium supplementation. The mean (SD) basal urinary Dpd excretion was 8.01 (3.02) nmol/mmol creatinine, which declined significantly (P = 0.012) to 6.95 (2.39) nmol/mmol creatinine after MCCM supplementation for 12 - 13 days (Fig. 1). Osteocalcin concentrations were also only measured...
in basal serum samples. The mean (SD) serum osteocalcin concentration after 13 days of MCCM supplementation was 2.82 (0.82) μg/l, which was not significantly different from the mean concentration of 2.59 (0.56) μg/l before supplementation was commenced. The effect of the second MCCM dose on mean plasma total calcium, plasma magnesium, ionised calcium and serum iPTH concentrations, as well as urinary calcium excretion, was not significantly different from that of the first MCCM dose. However, mean urinary magnesium excretion was significantly increased after the second MCCM dose (Table I).

Discussion

In this study, we assessed calcium bio-availability indirectly by monitoring urinary calcium excretion after consumption of an MCCM test dose. This approach is necessitated by the tight homeostatic control of circulating calcium concentrations by the parathyroid gland, which renders serum total calcium concentrations useless as an indicator of calcium bio-availability unless a radio-labelled calcium tracer is used. Compared with urinary calcium excretion after the consumption of water, we found significantly increased calcium excretion after a single dose of MCCM. This calciuric response was not the result of complex formation by urinary citrate, because administration of CMC did not have a significant effect on urine calcium excretion (Table I). The amount of calcium excreted upon MCCM administration is similar to that reported for 500 mg elemental calcium in the form of calcium citrate. Harvey reported an increase of 0.139 mg elemental calcium per mg creatinine (372.1 μmol/mmol creatinine) in the mean urinary excretion during the 4-hour period following calcium citrate administration. Compared with water, we found that the first dose of MCCM resulted in a mean increase in calcium excretion of 365.0 μmol/mmol creatinine. This suggests that MCCM has calcium delivery properties similar to those of calcium citrate and that the calcium delivery properties of MCCM are not negatively affected by the presence of 250 mg elemental magnesium. These observations are in agreement with a recent report by Fine and co-workers who demonstrated by the significant increases in mean plasma ionised calcium concentrations following the MCCM dose. The higher circulating plasma ionised calcium concentrations resulted in a profound and significant decline in circulating iPTH levels, which may be expected to reduce the process of bone resorption. The increase in plasma ionised calcium concentrations and the decline in PTH concentrations have been reported previously for higher oral doses of calcium (1 g) and are indicative of calcium absorptive capacity. It is noteworthy that the administration of the CMC control resulted in a significant decline in the plasma mean ionised calcium concentration (P < 0.001), while the mean iPTH concentration increased by 16.2% (P = 0.051; Table II). This phenomenon is presumably explained by the systemic alkalinising effect of citrate and malate. The equilibrium between albumin-bound and free calcium is shifted in the direction of complex formation with albumin by a higher blood pH, thus explaining the significant decline in plasma ionised calcium concentrations. When the ionised calcium concentrations were adjusted for pH, the observed changes failed to reach the conventional upper limit of statistical significance (Table II). It is not known whether this effect of citrate and malate has any implications for calcium absorption and metabolism.

Citrate and malate are normally metabolised to bicarbonate, which explains the significant increases in blood standard bicarbonate concentrations and pH after administration of either CMC or MCCM. Our results suggest that consumption of MCCM will not only supply additional dietary calcium, but may also partially neutralise the acidifying effect of the typical western acid-ash diet (i.e. a diet that, upon metabolism, generates a residue of acid), which causes excessive calcium losses and a negative calcium balance which may eventually contribute to osteoporosis. On the other hand it may be argued that, although statistically significant, the effect of MCCM on blood bicarbonate concentrations and pH are small and may be expected to have a negligible effect on endogenous acid production. Clinical studies, including detailed acid-base status assessments, are required to establish whether MCCM has advantages above other sources of calcium in the prevention of osteoporosis.

Based on urinary excretion rates of magnesium, it is concluded that MCCM is a bioavailable source of magnesium. Following a 2-week period during which MCCM (5 g/day) was consumed, the urinary magnesium excretion rate after a single MCCM test dose was significantly higher compared with the first MCCM test dose. This presumably reflects an increased saturation of the body magnesium stores as a result of daily MCCM supplementation. Although magnesium is an important component of the bone matrix, and although subnormal concentrations of magnesium have been demonstrated in trabecular bone of osteoporotic women, it remains unclear whether magnesium supplementation per se will slow the pathogenesis of osteoporosis. A few open trials have been completed which suggest that magnesium supplementation increases bone mineral density, but the mechanism of the effect induced by magnesium is still unknown. Considering the magnesium dependency of the PTH response to hypocalcaemia, it may well be that an adequate magnesium status is required to optimise the effect of magnesium supplementation. Controlled clinical trials are, however, required to evaluate the role of magnesium supplementation in osteoporosis prevention.

Serum concentrations of osteocalcin, a biochemical marker of bone formation, did not change significantly during the study, but urinary Dpd excretion, a biochemical marker of bone resorption, decreased significantly upon MCCM consumption. This indicates that daily use of the calcium/magnesium supplement slowed bone resorption, while it did not have a significant effect on the rate of bone formation over the study period. With regard to urinary Dpd excretion, the individual responses to MCCM consumption showed considerable variation. Fig. 1 indicates that those individuals with initial high levels of urinary Dpd excretion (i.e. high levels of bone resorption) showed relatively large


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REFERENCES


14. Mahaffee ME, Cooper CW, Ramp WK, Omittas DA. Magnesium promotes both parathyroid hormone secretion and adenoma S3 monophosphatase production in rat parathyroid tissues and reverses the inhibitory effects of calcium on adenylate cycle. Endocrinology 1982; 110: 487-495.


