

Calcium supplementation: effect on iron absorption¹⁻³

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ABSTRACT The influence of calcium supplements on the absorption of dietary nonheme iron and of iron supplements was evaluated in 61 normal volunteer subjects by use of a double-radioisotope technique. When taken without food, calcium carbonate did not inhibit the absorption of ferrous sulphate with doses of either 300 mg Ca and 37 mg Fe or 600 mg Ca and 18 mg Fe. However, at the latter levels, calcium citrate and calcium phosphate reduced iron absorption significantly by 49% and 62%, respectively. All calcium supplements inhibited absorption of the iron supplement when taken with food. The absorption of dietary nonheme iron was also inhibited by all three supplements. This inhibition was less pronounced from a meal of high iron availability and low calcium content (28%) than from a breakfast meal of low iron availability and high calcium content (55%). These results suggest that taking regular calcium supplements with meals makes it more difficult for women to meet their daily iron requirement. *Am J Clin Nutr* 1991;53:106-11.

KEY WORDS Iron absorption, calcium, supplementation

Introduction

The most common nutritional deficiencies now affecting adult women involve iron and calcium. The use of a daily calcium supplement by women in their childbearing years and beyond is believed to reduce the risk of postmenopausal osteoporosis. Iron supplementation is also widely recommended in adult women, particularly when iron requirements are increased because of pregnancy, lactation, or endurance training. When both iron and calcium supplements are indicated, compliance is improved when these supplements are taken together. However, recent clinical observations suggest that iron absorption from prenatal supplements is adversely affected by other minerals such as calcium (1) and that calcium supplementation reduces the absorption of dietary iron (2).

The present investigation was undertaken to assess more fully the effect of calcium supplements on iron absorption. We studied the effects of calcium carbonate, calcium citrate, and calcium phosphate, all of which are now widely used for calcium supplementation. We examined their effect on the absorption of nonheme food iron and the absorption of ferrous sulphate taken with or without food. Other variables included in our evaluation were the relative amounts of added calcium and iron, the iron status of the subjects, and the bioavailability of iron from the meal.

Subjects and methods

Subjects

The volunteer subjects included 28 women and 33 men between the ages of 20 and 39 y. All were in good health and denied a history of disorders known to influence iron absorption. None of the subjects were anemic, but eight had depleted iron stores as defined by a serum ferritin concentration $\leq 12 \mu\text{g/L}$. Written informed consent was obtained from each volunteer before the investigation and all experimental procedures were approved by the Human Subjects Committee at the University of Kansas Medical Center.

Iron-absorption measurements

Iron absorption was measured from four separate test meals in each subject by use of sequential ^{55}Fe and ^{59}Fe labels. All test meals were given between 0700 and 0900 after an overnight fast. Only water was permitted for 3 h after each test meal. The test meals were labeled with either 111 MBq ^{55}Fe or 37 MBq ^{59}Fe (New England Nuclear, North Billerica, MA). On the day preceding the first test, blood was drawn for measurement of packed cell volume, serum ferritin concentration (3), and background radioactivity. The first pair of test meals, tagged separately with either ^{55}Fe or ^{59}Fe , were then fed on the following two mornings. Fourteen days after the second test dose, blood was drawn for measurement of incorporated red cell radioactivity. The second pair of test meals, again labeled with either ^{55}Fe or ^{59}Fe , were fed on the next two mornings, and a final blood sample was obtained 2 wk later to measure the increase in red cell radioactivity. Measurements of blood radioactivity were performed on duplicate 10-mL specimens of whole blood by use of a modification of the method of Eakins and Brown (4). Percentage absorption was calculated on the basis of blood volume estimated from height and weight (5, 6). Red cell incorporation of absorbed radioactivity was assumed to be 80% in all subjects (7).

Preparation of test meals

Labeled iron supplements were prepared by crushing Feosol tablets (Smith, Kline, and French Laboratories, Philadelphia)

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TABLE 1
Effect of calcium carbonate (300 mg Ca) on absorption of ferrous sulphate (37 mg Fe) given with and without a hamburger meal

Subject (sex)	Age	Packed cell volume	Serum ferritin	Iron absorption (%)				Absorption ratio (+Ca/-Ca)	
				With food		Without food		With food	Without food
				-Ca	+Ca	-Ca	+Ca		
	<i>y</i>	%	$\mu\text{g/L}$	% of dose					
1 (F)	21	40	11	5.93	6.00	7.77	10.27	1.01	1.32
2 (F)	22	42	12	2.40	1.32	6.55	5.70	0.54	0.87
3 (F)	20	39	13	4.52	2.82	13.32	8.40	0.62	0.63
4 (F)	20	40	16	1.56	1.67	6.00	4.41	1.07	0.73
5 (F)	21	41	23	1.93	1.35	5.06	5.52	0.69	1.09
6 (F)	20	40	28	0.60	0.53	3.92	3.67	0.88	0.93
7 (F)	22	43	33	1.25	0.98	6.58	4.02	1.27	0.61
8 (F)	20	41	35	2.98	1.68	11.72	11.71	0.56	0.99
9 (F)	20	44	37	2.58	1.32	15.02	9.98	0.51	0.66
\bar{x} *	21	41	21	2.12	1.61†	7.68	6.50‡	0.76	0.85
-1 SEM			18	1.67	1.30	6.60	5.61	0.68	0.77
+1 SEM			25	2.69	2.01	8.95	7.53	0.85	0.92

* Geometric means except for age and packed cell volume.

† Significantly different from with-food value, without calcium, $P = 0.043$.

‡ Not significantly different from without-food value, without calcium, $P > 0.10$.

to a fine powder and mixing thoroughly with the radioactive label. The powder was then pressed through a 100-mesh screen three times and placed in a #4 gelatin capsule. The variation in radioactivity between different batches of labeled capsules was $< \pm 2\%$. Commercially available calcium supplements were given separately. Calcium carbonate was given as Caltrate (Lederle Laboratories, America Cyanamid, Pearl River, NY), calcium citrate was given as Citracal (Mission Pharmaceutical Co, San Antonio, TX), and calcium phosphate was given as Posture (Ayerst Laboratories, New York).

When assessing the effect of calcium supplements taken with food, two meals were selected to represent the extremes in iron bioavailability. The enhancing meal consisted of a hamburger patty (94 g) and bun (70 g). The meal contained 1708 kJ, 26 g protein, and 5.1 mg Fe, of which 1.4 mg was heme and 3.7 mg nonheme. When the absorption of the native nonheme iron was measured, this meal was tagged extrinsically by pipetting 0.5 mL 0.1 mol HCl/L containing 0.1 mg Fe as [^{55}Fe]chloride onto the bun (8). The inhibiting meal was a typical breakfast meal containing an egg, muffin, 40% bran flakes, sugar, 2% lowfat milk, and coffee (9). The meal weighed 562 g and contained 2467 kJ, 31 g protein, and 4.7 mg Fe. The meal was labeled extrinsically in the same manner as the enhancing meal.

Statistical analysis

Percentage absorption values and absorption ratios were converted to logarithms for statistical analysis and the results were reconverted as antilogarithms to recover the original units (10). Paired t tests were used to compare absorption from meals given with and without a calcium supplement by determining whether the mean log absorption ratio differed significantly from zero. Differences in mean absorption ratios between studies were evaluated by analysis of variance and by Sheffé's test. The

ABSTAT program was used for the statistical analyses (AndersonBell Corp, Parker, CO).

Results

In our initial study we examined the effect of adding a modest supplement of calcium carbonate (300 mg Ca) to a therapeutic dose of ferrous sulphate (37 mg Fe). When taken with the enhancing meal, iron absorption fell from 2.12% to 1.61%, a modest but significant 24% decrease ($t = 2.36$, $P = 0.043$) (Table 1). When the calcium and iron supplements were taken with water, mean absorption fell by only 15%, from 7.7% to 6.5% ($P > 0.10$). Because of the marginal inhibitory influence of calcium with these relative amounts of added calcium and iron, we used a higher level of Ca (600 mg) and a lower level of Fe (18 mg) in subsequent studies.

The next series of studies was performed with the same experimental design. The first of two studies with calcium carbonate was performed in a group of volunteers with low iron reserves as reflected by a mean serum ferritin of 24 $\mu\text{g/L}$ (Table 2). The addition of calcium carbonate to the hamburger meal reduced absorption from 13.0% to 7.3%, a significant 44% decrease ($P < 0.001$). As in the first study, no significant effect was seen when iron and calcium supplements were taken with water; a slight increase in iron absorption from 18.0% to 21.5% occurred. This same study was repeated in volunteers with normal iron reserves as indicated by a serum ferritin of 74 $\mu\text{g/L}$. Calcium carbonate produced a slight 16% decrease in iron absorption from 3.9% to 3.3% when taken with food and even less effect when taken with water. In neither case was the inhibitory effect statistically significant ($P > 0.10$). If the iron absorption ratios with and without calcium carbonate taken with food in subjects with normal and reduced iron stores are pooled, a mean ratio

TABLE 2
Effect of different calcium supplements (600 mg Ca) on absorption of ferrous sulphate (18 mg Fe) given with or without a hamburger meal

Subject (sex)	Age	Packed cell volume	Serum ferritin	Iron absorption (%)				Absorption ratio (+Ca/-Ca)	
				With food		Without food		With food	Without food
				-Ca	+Ca	-Ca	+Ca		
<i>y</i>	%	$\mu\text{g/L}$	% of dose						
Calcium carbonate (reduced iron stores)									
1 (F)	20	38	6	39.7	17.5	58.5	61.4	0.44	1.04
2 (F)	25	40	12	26.7	14.4	20.4	49.6	0.53	1.68
3 (F)	28	41	13	34.7	20.9	37.1	29.2	0.60	0.78
4 (F)	28	44	23	3.7	3.4	11.8	7.7	0.90	0.65
5 (F)	21	37	26	15.6	11.3	14.6	37.0	0.72	2.53
6 (F)	21	39	26	18.1	6.4	27.7	25.0	0.35	0.90
7 (F)	20	39	29	5.2	4.3	9.9	14.8	0.82	1.48
8 (M)	22	43	73	8.2	3.4	9.9	10.6	0.41	1.07
9 (F)	21	40	75	6.2	3.1	6.6	9.9	0.49	1.49
\bar{x}^*	23	40	24	13.0	7.3†	18.0	21.5‡	0.56	1.20
-1 SEM				9.7	5.6	14.1	16.7	0.50	1.04
+1 SEM				17.3	9.4	23.0	27.6	0.63	1.38
Calcium carbonate (normal iron stores)									
1 (M)	23	44	19	34.0	25.6	41.1	28.3	0.75	0.68
2 (M)	22	45	25	7.5	8.0	8.9	10.1	1.06	1.13
3 (M)	23	49	75	11.4	6.6	12.5	11.0	0.57	0.88
4 (M)	25	46	80	1.6	3.1	12.7	8.9	1.93	0.69
5 (M)	24	46	95	2.5	1.1	6.4	7.7	0.44	1.20
6 (M)	22	44	96	2.2	0.8	6.2	5.2	0.36	0.83
7 (M)	23	46	98	3.6	4.3	9.9	11.9	1.19	1.21
8 (M)	23	47	104	1.8	1.6	5.0	5.8	0.92	1.16
9 (M)	23	45	115	2.3	2.2	9.2	6.9	0.95	0.74
10 (M)	21	45	171	2.2	2.5	12.4	9.7	1.16	0.78
\bar{x}^*	23	46	74	3.9	3.3§	10.3	9.4‡	0.84	0.91
-1 SEM				2.8	2.4	8.5	8.1	0.72	0.85
+1 SEM				5.3	4.5	12.3	10.9	0.99	0.98
Calcium citrate									
1 (M)	23	41	28	6.9	3.8	15.7	6.7	0.67	0.42
2 (F)	22	44	33	12.2	10.1	19.5	5.3	0.82	0.27
3 (F)	26	40	46	4.5	5.0	12.9	6.5	1.11	0.50
4 (M)	22	46	54	13.6	2.6	11.4	3.6	0.19	0.31
5 (M)	23	41	56	30.1	20.4	21.9	23.7	0.67	1.08
6 (M)	22	44	64	18.5	11.0	10.0	8.4	0.59	0.83
7 (M)	22	44	164	3.9	2.8	5.9	3.3	0.71	0.55
\bar{x}^*	23	43	54	10.1	6.1	12.9	6.6¶	0.60	0.51
-1 SEM				7.6	4.5	10.9	5.2	0.49	0.43
+1 SEM				13.5	8.2	15.2	8.5	0.74	0.62
Calcium phosphate									
1 (M)	28	43	47	14.9	2.9	19.4	4.9	0.19	0.25
2 (F)	24	39	50	2.8	1.2	15.6	5.3	0.42	0.33
3 (M)	23	46	66	10.1	2.1	24.4	5.4	0.20	0.22
4 (M)	23	46	79	10.1	5.7	29.1	13.1	0.56	0.44
5 (M)	26	47	96	8.1	8.4	23.4	15.3	1.03	0.65
6 (M)	23	43	105	8.7	7.1	12.9	3.9	0.81	0.30
7 (M)	24	43	108	3.8	1.3	4.1	2.6	0.33	0.61
\bar{x}^*	24	44	75	7.3	3.2**	16.0	6.0††	0.43	0.38
-1 SEM				5.8	2.3	12.5	4.7	0.34	0.32
+1 SEM				9.2	4.3	20.5	7.6	0.55	0.44

* Geometric means except for age and packed cell volume.

†** Significantly different from with-food value, without calcium: † $P < 0.001$, ** $P = 0.015$.

‡ Not significantly different from without-food value, without calcium, $P > 0.10$.

§|| Not significantly different from with-food value, without calcium: § $P > 0.10$, || $P = 0.058$.

¶†† Significantly different from without-food value, without calcium: ¶ $P = 0.013$, †† $P < 0.001$.

TABLE 3
Comparison of the effect of different calcium supplements* (600 mg Ca) absorption of nonheme iron from enhancing and inhibitory meals

Subject (sex)	Age	Packed cell volume	Serum ferritin	Iron absorption (%)						
				No added calcium	With			Absorption ratio (+Ca/-Ca)		
					Carbonate	Citrate	Phosphate	Carbonate	Citrate	Phosphate
	y	%	µg/L	% of dose						
Enhancing meal (with meat)										
1 (F)	22	37	5	33.1	21.0	31.3	21.5	0.63	0.94	0.64
2 (F)	22	37	11	25.8	21.0	45.6	43.8	0.81	1.76	1.69
3 (F)	23	39	14	30.5	31.0	26.1	9.9	1.01	0.86	0.32
4 (F)	22	39	24	36.2	29.0	15.0	21.3	0.80	0.41	0.58
5 (M)	24	44	43	8.6	5.8	6.2	4.9	0.66	0.72	0.56
6 (F)	22	41	54	13.5	7.9	11.0	7.7	0.58	0.81	0.57
7 (M)	24	44	60	12.4	5.1	5.1	3.0	0.40	0.40	0.24
8 (M)	23	46	80	5.3	3.0	6.7	4.4	0.57	1.27	0.83
9 (M)	27	46	184	1.8	1.2	3.7	2.3	0.66	2.00	1.23
10 (M)	26	49	409	14.3	12.1	12.3	6.3	0.84	0.85	0.44
\bar{x} *	23	42	42	13.4	9.1†	11.9‡	8.2§	0.68	0.89	0.61
-1 SEM				10.0	6.5	9.2	6.1	0.63	0.75	0.51
+1 SEM				18.1	12.8	15.5	11.1	0.74	1.05	0.74
Inhibiting meal (no meat)										
1 (F)	24	40	12	4.7	4.8	1.9	1.7	1.03	0.40	0.35
2 (F)	22	38	12	1.6	1.1	1.1	0.6	0.70	0.59	0.37
3 (F)	30	39	32	5.0	4.8	1.4	0.6	0.95	0.28	0.12
4 (M)	23	43	56	0.5	0.4	0.2	0.3	0.71	0.32	0.47
5 (M)	25	44	79	0.8	0.6	0.5	0.4	0.75	0.65	0.49
6 (M)	22	48	126	0.7	0.5	0.4	0.5	0.63	0.50	0.72
7 (M)	20	46	127	0.4	0.3	0.6	0.5	0.77	1.71	1.28
8 (M)	39	47	200	0.4	0.1	0.2	0.1	0.13	0.40	0.21
9 (M)	22	43	359	2.9	1.0	0.3	0.6	0.32	0.09	0.19
\bar{x} *	25	43	66	1.2	0.7	0.5¶	0.4¶	0.58	0.43	0.37
-1 SEM				0.8	0.4	0.4	0.3	0.47	0.33	0.29
+1 SEM				1.7	1.1	0.7	0.6	0.72	0.56	0.47

* Geometric means except for age and packed cell volume.

†§||¶ Significantly different from no-added-calcium value: † $P = 0.001$; § $P = 0.03$, || $P < 0.05$, ¶ $P < 0.01$.

‡ Not significantly different from no-added-calcium value, $P > 0.10$.

of 0.69 is obtained, which indicates significant inhibition ($P < 0.01$).

The same protocol was used to evaluate the effect of calcium citrate and calcium carbonate on the absorption of ferrous sulphate. Calcium citrate reduced iron absorption from 10.1% to 6.1% when taken with food, but this 40% decrease was not significant ($P = 0.058$) (Table 2). On the other hand, when taken without food, calcium citrate reduced absorption by 49%, from 12.9% to 6.6% ($P < 0.013$). The greatest inhibition occurred with calcium phosphate, which reduced absorption of ferrous sulphate when taken with food by 57%, from 7.3% to 3.2% ($P = 0.015$), and when taken with water by 62%, from 16.0% to 6.0% ($P < 0.001$). Thus, the reduction in iron absorption by calcium phosphate exceeded 50% in both cases.

When the results of these studies are taken together, it is apparent that the effect of calcium supplements on the absorption of an iron supplement depends on whether they are taken with food. Without food, calcium carbonate has no inhibitory effect on the absorption of ferrous sulphate, whereas calcium citrate

and calcium phosphate are both inhibitory. All three forms inhibit the absorption of an iron supplement if taken with food, although the degree of inhibition was not statistically significant with calcium citrate. When taken with food, the pooled mean absorption ratio with and without added calcium was 0.53 (± 1 SEM, 0.47-0.59), reflecting a highly significant inhibitory effect ($t = 5.26$, $P < 0.0001$).

In the final series of studies, we examined the effect of calcium supplementation on dietary nonheme iron absorption. Mean absorption from the enhancing meal taken without added calcium was 13.4% (Table 3). Iron absorption was reduced significantly by 32% with calcium carbonate ($P < 0.001$) and 39% with calcium phosphate ($P < 0.03$) but by only 11% with calcium citrate ($P > 0.10$). However, when the mean absorption ratios of the three calcium forms were compared by analysis of variance, the differences were not significant ($F = 1.63$, $P = 0.21$). The pooled mean absorption ratio of 0.71 (± 1 SEM, 0.65-0.78) indicated a highly significant inhibiting effect of calcium ($t = 3.78$, $P < 0.0001$).

The inhibiting effect of calcium supplements on food iron absorption was more pronounced with a breakfast meal containing several known inhibitors of iron absorption. When fed without calcium, mean absorption from this meal was only 1.2% as compared with 13.4% from the hamburger meal (Table 3). The degree of inhibition was similar for all three calcium supplements: 32% with calcium carbonate ($P < 0.05$), 57% with calcium citrate ($P < 0.01$), and 63% with calcium phosphate ($P < 0.01$). When these results were compared by analysis of variance, however, differences among the three calcium supplements were not significant ($F = 0.9$, $P = 0.41$). The pooled mean absorption ratio was $0.45 (\pm 1 \text{ SEM}, 0.39-0.52)$, indicating a highly significant inhibiting effect ($t = 5.79$, $P < 0.0001$). The degree of inhibition with the breakfast meal was also significantly greater than with the hamburger meal ($t = 2.871$, $P = 0.003$). Thus, the inhibiting effect of calcium on nonheme iron absorption is similar with all three supplements and is significantly greater when the meal itself contains poorly available iron (Fig 1).

Discussion

Despite investigation for more than a half century, the effect of calcium on iron absorption is still unclear. The majority of investigations have been performed on laboratory animals and these findings were recently reviewed (11). There is surprisingly little clinical information, particularly about the effect of the larger amounts of calcium used for supplementation. At the level of calcium commonly used for supplementation, an inhibitory effect was demonstrated by Seligman et al (1), who added different forms of calcium to various prenatal multivitamin and mineral supplements. Iron absorption was determined indirectly in healthy, fasting women from the postabsorptive rise in serum iron, a method that cannot be used to measure food iron absorption. A significant decrease in iron absorption from 9.0% to 6.8% was observed when 300 mg Ca as calcium carbonate was added to 65 mg Fe as ferrous fumarate.

These results differed from our present study, where an insignificant 15% decline in iron absorption occurred when 300 mg Ca as calcium carbonate was given with 37 mg Fe as ferrous sulphate. Moreover, no effect was seen when the amount of calcium was doubled and the iron halved. On the other hand, both calcium citrate and calcium phosphate decreased absorption of ferrous sulphate when given with water. There are several possible explanations for the difference in findings in these two studies. Our iron and calcium supplements were given in separate capsules, whereas in the previous report these minerals were formulated in the same preparation. Their commercial prenatal preparation contained several other minerals and vitamins, some of which may have augmented any inhibitory effect of calcium carbonate. It is also possible that ferrous fumarate, which was used in the prenatal supplement, is more influenced by calcium carbonate than is the ferrous sulphate evaluated in our studies. At neutral pH, ferrous fumarate is far less soluble in water than is ferrous sulphate, although it dissolves rapidly at the more acid pH of gastric juice.

Whereas calcium carbonate failed to inhibit iron absorption when taken with water, we detected no obvious difference in the inhibiting effects of calcium carbonate, calcium citrate, and calcium phosphate when taken with food. A similar inhibiting effect of these supplements was observed with meals of both high and low iron availability and with or without an added ferrous sul-

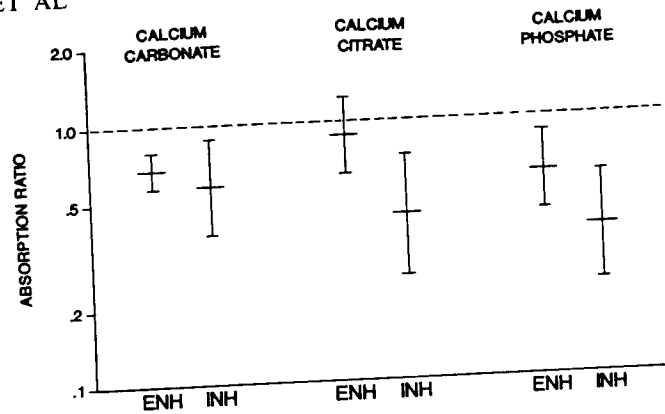



FIG 1. Effect of calcium supplements (600 mg Ca) on nonheme iron absorption from an enhancing (ENH) and inhibiting meal (INH). Mean absorption ratios ± 2 SEM are shown.

phate supplement. The degree of inhibition was similar to that observed when a breakfast meal was fed to postmenopausal women (2). In this study, basal absorption of 6.3% was reduced by 57% when 500 mg Ca as calcium carbonate was added and by 54% when the same amount of calcium was added as hydroxyapatite. This degree of inhibition was almost identical to that observed with our inhibitory meal in the present study; inhibition ranged between 42% and 63%, with a pooled mean of 55%.

An unexpected finding in the present study was that the degree of inhibition in nonheme iron absorption varied with the nature of the meal. The relative inhibition was considerably less with a hamburger meal that promoted nonheme iron absorption, compared with a breakfast meal that contained several inhibitors of iron absorption. There are several possible explanations for the differences in inhibition with these two meals. It is possible that the inhibitory effect of calcium may have been partially offset by the meat in the hamburger meal, which facilitated the absorption of nonheme iron (12). The estimated calcium content of the two meals also differed markedly, 597 mg for the breakfast meal as compared with 141 mg for the hamburger meal. If the inhibitory effect of calcium is proportional to the amount contained in the meal and if dietary and nondietary calcium are comparable in their effect, a greater inhibition would be expected with the breakfast meal. Finally, the ability to quantify reliably an inhibitory effect with the breakfast meal is less because of the low basal absorption of 1.2% as compared with 13.4% for the hamburger meal. The difference in the inhibiting effect of calcium with different meals is important in predicting the long-term effects of regular calcium supplementation on iron balance. Although the inhibiting effect of calcium is greater with a meal that inhibits absorption, iron absorption from our breakfast meal is too low to account for significant quantities of absorbed iron.

Predictions about the potential influence of regular calcium supplementation on iron balance must take into account the specific fraction of dietary iron and the number of meals with which the calcium supplements are consumed. Heme iron is believed to account for approximately one-third of the absorbed dietary iron, and because dietary ligands do not influence heme absorption, any inhibiting effect of calcium supplements is limited to nonheme dietary iron. Recent studies showed that 0.73 mg of nonheme iron is absorbed daily by women with depleted

iron stores (13). Thus, only 0.1–0.2 mg would be furnished by a breakfast meal containing numerous inhibitors of iron assimilation. If calcium supplements are taken only with a breakfast meal, reduction in absorbed nonheme dietary iron would be only 10–15%/d. A decrease of 20–30% could occur if calcium supplements are ingested with each meal of the day. When calcium carbonate was taken with food in the present study, the inhibitory effect was greater in women with reduced iron stores (Table 2).

Our present observations permit some tentative conclusions about the effect of calcium supplementation on iron balance. If combined iron and calcium supplementation is required, no adverse effects on iron absorption will occur if calcium carbonate is used and the supplements are taken between meals. If both are taken with food, the calcium supplement reduces the absorption of ferrous sulphate by one-third. Calcium supplements also inhibit the absorption of dietary nonheme iron. All forms of calcium share this property, but the degree of inhibition varies with the nature of the meal. The relative inhibition is greater with a breakfast meal of low iron availability (55% inhibition) than with a hamburger meal of high iron availability (28% inhibition). If taken with meals, calcium supplements used regularly may make it more difficult to meet daily iron requirements. 

References

1. Seligman PA, Caskey JH, Frazier JL, Zucker RM, Podell ER, Allen RH. Measurements of iron absorption from prenatal multivitamin-mineral supplements. *Obstet Gynecol* 1983;61:356–62.
2. Dawson-Hughes B, Seligson FH, Hughes VA. Effects of calcium carbonate and hydroxyapatite on zinc and iron retention in postmenopausal women. *Am J Clin Nutr* 1986;44:83–8.
3. Flowers CA, Kuizon M, Beard JL, Skikne BS, Covell AM, Cook JD. A serum ferritin assay for prevalence studies of iron deficiency. *Am J Hematol* 1986;23:141–51.
4. Eakins JD, Brown DA. An improved method for the simultaneous determination of iron-55 and iron-59 in blood by liquid scintillation counting. *Int J Appl Radiat Isot* 1966;17:391–7.
5. Wennesland R, Brown E, Hopper J Jr, et al. Red cell, plasma and blood volume in healthy men measured by radiochromium (Cr51) cell tagging and hematocrit: influence of age, somatotype and habits of physical activity on variance after regression of volumes to height and weight combined. *J Clin Invest* 1959;38:1065–77.
6. Brown E, Hopper J Jr, Hodges JL Jr, Bradley B, Wennesland R, Yamauchi H. Red cell, plasma, and blood volume in healthy women measured by radiochromium cell-labeling and hematocrit. *J Clin Invest* 1962;41:2182–90.
7. Hosain F, Marsaglia G, Finch CA. Blood ferrokinetics in normal man. *J Clin Invest* 1967;46:1–9.
8. Cook JD, Layrisse M, Martinez-Torres C, Walker R, Monsen E, Finch CA. Food iron absorption measured by an extrinsic tag. *J Clin Invest* 1972;51:805–15.
9. Cook JD, Lipschitz DA, Skikne BS. Absorption of controlled-release iron. *Clin Pharmacol Ther* 1982;32:531–9.
10. Cook JD, Layrisse M, Finch CA. The measurement of iron absorption. *Blood* 1969;33:421–9.
11. Barton JC, Conrad ME, Parmley RT. Calcium inhibition of inorganic iron absorption in rats. *Gastroenterology* 1983;84:90–101.
12. Bothwell TH, Charlton RW, Cook JD, Finch CA. *Iron metabolism in man*. Oxford, England: Blackwell Scientific, 1979.
13. Lynch SR, Skikne BS, Cook JD. Food iron absorption in idiopathic hemochromatosis. *Blood* 1989;74:2187–93.