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Calcium

DESCRIPTION

Calcium is an essential mineral with a wide range of biological roles. Apart from being a major constituent of bones and teeth, calcium is crucial for muscle contraction, nerve conduction, the beating of the heart, blood coagulation, glandular secretion, the production of energy and the maintenance of immune function, among other things. Calcium is an alkaline-earth metal with atomic number 20 and an atomic mass of 40.08 daltons. Its atomic symbol is Ca.

Calcium is found in bone and teeth primarily in the form of the calcium phosphate compound hydroxyapatite. The molecular formula of hydroxyapatite is $Ca_{10}(PO_4)_6(OH)_2$. Over 99% of the total body calcium is found in bone and teeth, and calcium makes up from 1% to 2% of adult body weight.

Milk products are the most calcium-dense foods. Other foods rich in calcium include the vegetables collard greens, Chinese cabbage, mustard greens, broccoli and bok choy, as well as tofu and sardines with bones included. About 25% of women in the United States take calcium supplements. The average intake of calcium in the American diet is approximately 800 milligrams daily. Calcium intake is typically higher in males than it is in females.

ACTIONS AND PHARMACOLOGY

ACTIONS

Calcium has anti-osteoporotic activity. It may also have anticarcinogenic, antihypertensive and hypocholesterolemic activity.

MECHANISM OF ACTION

Inadequate calcium intake results in reduced bone mass and osteoporosis. Calcium exists in bone primarily in the form of hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$). Hydroxyapatite comprises approximately 40% of the weight of bone. The skeleton has an obvious structural requirement for calcium. The skeleton also serves as a reservoir for calcium.

A number of studies suggest that calcium may reduce the risk of colorectal cancer. Calcium supplementation has been found to reduce colonic mucosal proliferation. Greater colonic mucosal proliferation is observed in those at high risk for colon cancer when compared with those at low risk. Calcium ions may precipitate bile acids and fatty acids that can stimulate the proliferation of colon cells.

Calcium supplementation has been found to have a modest effect on the reduction of systolic blood pressure in those with hypertension. Diastolic blood pressure does not appear to be affected by calcium, and calcium does not affect blood pressure in normotensives. The mechanism of the possible systolic blood pressure-lowering effect of supplemental calcium is unclear.

Some, but not all, studies have found supplemental calcium to lower serum cholesterol levels. A mechanism of this possible effect may be the binding of calcium ions with bile acids to form insoluble soaps, thus removing cholesterol entering the gut via the enterohepatic circulation.

PHARMACOKINETICS

Calcium is absorbed from the small intestine by both active and passive mechanisms. At low and moderate intakes of calcium, calcium is absorbed via active transfer. Active transfer depends on the action of the active form of vitamin D,1,25-dihydroxycholecalciferol or $1,25(OH)_2\ D_3$. Vitamin D-induced calcium transport involves the synthesis of the calcium-binding protein, calbindin. Calbindin serves as a calcium translocator. It also serves as a cytosolic calcium buffer. Calcium is typically freed from calcium complexes during digestion and is released in a soluble and probably ionized form for absorption. Low molecular weight complexes, such as calcium carbonate, may be absorbed intact.

As calcium intakes increase, the active transfer mechanism becomes saturated and an increasing proportion of calcium is absorbed via passive diffusion.

The absorption efficiency of calcium varies throughout the life span. It is highest during infancy when it is about 60%. In prepubertal children, it is about 28%. During early puberty, at the time of the growth spurt, it increases to about 34% and then drops to 25% two years later where it remains for several years. Absorption efficacy increases during the last two trimesters of pregnancy. It does decline with aging. In postmenopausal women, fractional absorption of calcium declines on the average of 0.21% yearly. Men lose absorption efficiency at about the same rate as women.

Absorption efficiency appears to vary with the different calcium complexes. In one study, absorption efficiency from a 250 milligram dose of calcium citrate malate was found to be 35%; from calcium carbonate, 27%; and from tricalcium phosphate, 25%. For comparison, calcium absorption efficiency from milk was found to be 29%. Some, but not all, studies suggest that calcium is more efficiently absorbed from calcium citrate and calcium citrate malate than it is from calcium carbonate. The efficiency of absorption of calcium from a calcium supplement is greatest when calcium is taken at doses of 500 milligrams or lower. Individuals with

achlorhydria absorb calcium from calcium carbonate poorly unless the calcium carbonate supplement is taken with food.

Calcium that is unabsorbed from the intestine is excreted in the feces. Greater than 98% of calcium from the glomerular filtrate is reabsorbed. Renal reabsorption is primarily regulated by parathyroid hormone or PTH.

The colon plays an important role in calcium absorption after resection of the small intestine.

Approximately 40% of calcium in the plasma is bound to proteins, primarily albumin; about 50% of calcium in the plasma is diffusible ionic calcium and about 10% is diffusible, but is complexed with such anions as phosphate and citrate.

INDICATIONS AND USAGE

Calcium has long been assumed to be useful in preventing and treating osteoporosis and being beneficial for bone health in general. Recently, some highly publicized studies have cast some doubts on these claims, presenting conflicting and now controversial findings. The preponderance of evidence, however, continues to suggest an effective preventive role for calcium in osteoporosis in the aging population. Similarly, early findings that calcium significantly reduces risk of colorectal cancer were not supported by more-recent research. Again, however, there may be more evidence in support of a positive role than a neutral role; the issue is unresolved. Evidence continues to accumulate that calcium may help control blood pressure. There is also some evidence it may help reduce the risk of preeclampsia and maternal death during pregnancy. On the other hand, a recent study reported a higher incidence of myocardial infarction among healthy postmenopausal women who were taking calcium supplements (compared with placebo controls). There is weak and mixed evidence that calcium favorably affects lipids. An association has been made between higher intakes of calcium and lower incidence of stroke among women. A preliminary study some years ago suggested that calcium may help reduce the risk of obesity.

RESEARCH SUMMARY

In a review several years ago of 52 intervention trials investigating calcium's effects on osteoporosis, all but two were said to have shown beneficial effects, including better bone balance, greater bone gain during growth, reduced bone loss in the elderly and reduced risk of fracture. Observational studies have also, for the most part, associated higher calcium intake with enhanced bone health. Most of the intervention trials utilized calcium supplements; some used dairy products as the source of calcium. Most of these studies reported that high calcium intake augmented the osteoprotective effects of estrogen.

Some older studies have suggested that calcium citrate is better absorbed than calcium carbonate and that the citrate form might thus be more effective in helping to prevent or ameliorate osteoporosis. An analysis of 15 randomized trials concluded that calcium citrate was absorbed 22% to 27% better than calcium carbonate, whether taken on an empty stomach or with food. More research will be needed, however, to demonstrate conclusively that calcium citrate is more beneficial than calcium carbonate in osteoporosis.

Calcium has shown benefit in individuals who have lost bone mineral density due to long term corticosteroid therapy. In a double-blind, placebo-controlled study of subjects with rheumatoid arthritis, many of whom were being treated with corticosteroids, a combination of 1,000 milligrams of calcium carbonate and 500 IUs of vitamin D_3 daily was found to confer significant benefits. While subjects receiving placebo and prednisone lost bone mineral density in the lumbar spine and trochanter at a rate of 2% and 0.9%, respectively, per year, those getting prednisone and calcium gained bone mineral density in the lumbar spine and trochanter at a rate of 0.72% and 0.85% per year, respectively. No calcium-related improvements were seen, however, at any site in subjects who did not receive corticosteroids.

Recently, the results of some of these earlier studies have been partially contradicted by some, but not all, new research. In one major inquiry, 36,282 postmenopausal women, aged 50 to 79 years and enrolled in the Women's Health Initiative, were recruited for random assignment to either placebo or 1,000 milligrams of elemental calcium as calcium carbonate with 400 IU of vitamin D daily. The researchers sought to see what effect the calcium/D supplementation might have on risk of fractures in this aging population. Bone density was measured and fracture incidence followed up for seven years. A small but significant improvement in hip bone density was noted in the calcium/D group but not in the placebo group. The supplement group, however, had no fewer fractures than the placebo group. Incidence of kidney stones was higher in the supplement group. The result was unexpected, and the authors conceded that even a study involving this large a group of subjects with seven-year follow-up may not have been large enough or long enough in duration to detect at least a small but potentially significant benefit. Indeed, they reported that in a subgroup of women, over 60 years of age and judged by various measures to have a higher absolute risk of hip fracture, the calcium/D supplementation did significantly reduce the risk of hip fracture. Additionally, women who most closely complied with the supplement regimen had lower risk of fracture than those with lower levels of compliance.

An editorial accompanying publication of this important study in *The New England Journal of Medicine* noted that calcium supplements are the biggest seller in the multi-billion-dollar dietary-supplement marketplace, accounting for almost a billion dollars in sales per year in the United States alone. Thus, on financial as well as scientific grounds, the issue of what benefits, if any, accrue in terms of bone health warrants and demands close scrutiny. After taking into account the various weaknesses of the study, the editorialist nonetheless concluded that "calcium with vitamin D supplementation is not an effective means of preventing fractures in this population." Even if certain subgroups may benefit from this supplementation, the editorial cautioned women—and others at risk of fracture—about relying on this supplementation to significantly protect them: "Many women believe that they are completely protected against the development of osteoporosis if they are taking these supplements. This study should help correct this important misconception and allow more women to receive optimal therapy for bone health." Postmenopausal women, the editorial continued, might well be advised to continue taking the recommended daily levels of calcium and vitamin D (derived either through diet or supplementation or both), "but one message is clear: calcium with vitamin D supplementation by itself is not enough to ensure optimal bone health."

Some review authors concluded that there is evidence that calcium/vitamin D supplementation can be useful in preventing and ameliorating osteoporosis in the following groups: 1) patients with documented osteoporosis receiving antiresorptive or anabolic treatment, 2) individuals with or at high risk of calcium and/or vitamin D insufficiencies, especially elderly men and women, and 3) patients receiving glucocorticoids. They said benefits are most apparent when subjects are supplemented with 1,000-1,200 milligrams daily of elemental calcium combined with 800 IU daily of vitamin D. Level of compliance, they found, correlates with level of efficacy.

In a recent, double-blind, randomized trial, 930 generally healthy participants (mostly men, mean age: 61 years) received 1,200 milligrams of calcium daily for four years or placebo. Follow-up was for a mean of 10.8 years. The supplementation was found to significantly reduce the risk of all fractures and especially of minimal trauma fractures. The protective effect gradually dissipated after supplementation was discontinued. One of the purposes of this study was to see if calcium alone—not combined with vitamin D—could still exert bone-protective effects.

A recent meta-analysis published in *The Lancet* found support for the use of both calcium alone and calcium in combination with vitamin D in the preventive treatment of osteoporosis in people 50 years or older. This important meta-analysis was based upon data from 29 randomized trials involving 63,897 subjects. Main outcomes analyzed were fractures of all types and percentage change of bone-mineral density from baseline. A 12% reduction in risk of fractures of all types was reported. Bone-mineral density improvement was significantly associated with the supplementation, as measured at both the hip and the spine. Fracture-risk reduction was significantly correlated with compliance in these studies. And treatment effect was better with calcium doses of 1,200 milligrams or more daily than with doses lower than that; similarly, better results were consistently seen when vitamin D doses were 800 IU or greater. They found that, overall, calcium by itself was as effective as calcium with D. But in some subgroups of individuals (institutionalized elderly and those with clear vitamin D deficiency), the combination was more efficacious. Another meta-analysis, it should be noted, recently concluded that vitamin D is only effective in reducing risk of hip fracture when calcium is combined with it. The authors of *The Lancet* meta-analysis concluded that it is likely that calcium supplementation among postmenopausal women is cost-effective and that cost-effectiveness is likely to be better still in high-risk subjects who optimally comply with supplementation.

An editorial accompanying publication of this meta-analysis in *The Lancet* took note of some of the conflicting findings of other studies and the assertion by some authorities that calcium, with or without vitamin D, should not be systematically recommended for the primary or secondary prevention of fracture in the elderly. The editorial writer asserted that "most of these studies had poor long-term adherence to study drug." The editorial pointed out that the meta-analysis found that 50-60% of participants in the studies analyzed became non-compliant in taking their medication/supplementation properly. But in that subpopulation, where at least 80% remained compliant, the level of risk reduction was double that of those who were poorly compliant. The editorial found the cost-effectiveness conclusions of the meta-analysis encouraging but not definitive and concluded that these preliminary observations on cost-effectiveness emphasize "the need for extensive and sophisticated health-economic analyses to assess the incremental cost-effectiveness ratio of calcium or calcium with vitamin D supplementation in various doses, regimens, populations and settings."

An inverse relationship has been noted in epidemiological studies between colon cancer incidence and calcium intake. In the four-year, multicenter Calcium Polyp Prevention study, calcium supplementation was associated with a significant reduction in the risk of recurrent colorectal adenomas. This double-blind, randomized trial enrolled 930 subjects with a history of colorectal adenomas. Mean age

was 61, and 72% of the subjects were men. Calcium was supplied in the carbonate form in a dose of 1,200 milligrams of elemental calcium daily. Follow-up continued for four years after initial examination.

Some other intervention trials, as well as several experimental studies, have provided further support for calcium benefit in modulating the rate of human colon cell proliferation and reducing the rate of colonic adematous polyps. It should be noted, however, that while many positive significant results have been reported, reduction in adenoma incidence has generally been modest in these studies.

More recently, some large studies and reviews have yielded far less promising results. One meta-analysis—while discerning some evidence in well-designed double-blind, placebo-controlled studies that calcium supplementation (1,200 milligrams daily for four years in one study, 2,000 milligrams daily for three years in another study) might confer a "moderate" preventive effect against colorectal adenomatous polyps—nonetheless concluded that "this does not constitute sufficient evidence to recommend the general use of calcium supplements to prevent colorectal cancer." In another recent study involving 36,282 postmenopausal women from 40 Women's Health Initiative centers, subjects were randomized to receive 500 mg of elemental calcium and 400 IU of vitamin D daily or placebo for an average of seven years. The supplementation was found to have no effect on the incidence of colorectal cancer in this group of postmenopausal women. The researchers conceded that, given the long latency associated with the development of colorectal cancer and the relatively short follow-up period, a significant effect could still not be entirely ruled out. Follow-up is ongoing to further assess this possibility. Some have criticized the study for using a dosage of both calcium and vitamin D that they believe is too low to deliver a significant effect; this shortcoming was acknowledged, as well, in an editorial accompanying publication of this paper in *The New England Journal of Medicine.*

There is some preliminary evidence that calcium supplementation may help some with PMS. A pilot study suggested that calcium might diminish some PMS symptoms. Subsequently, a placebo-controlled, multicenter study produced results showing that calcium-supplemented women had an overall reduction of 48% in severity of PMS symptoms, compared with a 30% reduction in those on placebo. Those in the calcium group reported a 54% reduction in aches and pains, compared with a 15% increase in pains reported by the placebo group. One of the researchers has speculated that women with PMS may have a functional hypocalcemia in which urine and blood levels of calcium are normal—but only because abnormally high levels of parathyroid hormone constantly extract calcium from bone. More research is needed.

In a recent, randomized, double-blind, placebo-controlled study of the effects of calcium supplementation on serum cholesterol and blood pressure in 193 men and women aged 30 to 74 years, treatment with 1 and 2 grams daily of calcium for four months conferred no significant benefits, compared with placebo. No significant effects were seen with respect to blood pressure, total or HDL-cholesterol levels. In some earlier trials, however, some modest hypocholesterolemic effects were observed. And in an analysis of 14 studies, calcium supplementation in women (1.5 to 2 grams daily) was associated with a reduction of 5.40 mmHg in systolic blood pressure and a reduction of 3.44 mmHg in diastolic blood pressure, compared with controls. Some associated but inconclusive reduction in the incidence of preterm delivery, cesarean delivery, intrauterine growth retardation, perinatal death and preeclampsia has been reported.

In more recent work, one study found that intakes of low-fat dairy products, calcium and vitamin D were each inversely correlated with risk of hypertension in middle-aged and older women. A meta-analysis of 40 randomized, controlled studies found that a mean daily dose of 1,200 mg of calcium reduced systolic blood pressure by 1.86 mmHg and diastolic blood pressure by 0.99 mmHg. Greater improvement was seen in those with relatively low calcium intake at baseline. Those involved in the Dietary Approaches to Stop Hypertension Study (DASH), a large and well-designed inquiry, continue to stress the need for adequate dietary calcium intake via dairy products. Another recent study showed that calcium supplementation (1.5-2 grams daily) reduced the risk of high blood pressure, preeclampsia and maternal death or serious morbidity among women studied. The authors reported that calcium supplementation during pregnancy reduced the risk of preeclampsia by about half and was especially effective among those women with low calcium intake at baseline.

Yet another recent randomized, double-blind, placebo-controlled study reported an upward trend in cardiovascular event rates, including heart attack, in healthy postmenopausal women given calcium supplementation, compared with those receiving placebo. Mean age of subjects was 74. More research is clearly warranted to see if this negative finding can be confirmed.

In the ongoing Nurse's Health Study, supplementary intake of 400 or more milligrams daily of calcium has been associated with a significantly reduced risk of stroke among women. Supplementary intakes higher than 600 milligrams daily did not appear to confer further benefit. Authors of the study hypothesized that a possible hypocholesterolemic

effect or some anti-clotting mechanism might account for the protective association observed in this population. Magnesium and potassium intakes were not associated with reduced risk of stroke in this study, although they have been thus associated in some other studies.

One group of researchers has recently reported that increasing the dietary calcium of obese subjects for one year produced a 4.9 kilogram loss of body fat. Experiments in mice showed that high calcium diets could reduce weight gain and foot pad mass by 26% to 39%. The same researchers examined epidemiological data in which they found a significant association between higher levels of body fat and lower intake of calcium. They concluded that "increasing dietary calcium suppresses adipocyte intracellular calcium and thereby modulates energy metabolism and attenuates obesity risk."

Prior laboratory research has shown that increased adipocyte intracellular calcium produces both stimulation of lipogenesis and inhibition of lipolysis. The high-calcium diets used in the studies of mice produced a 51% inhibition of adipocyte fatty acid synthase expression and activity and a 3.4- to 5.2-fold increase in lipolysis. More research is warranted.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Calcium supplementation is contraindicated in those with hypercalcemia. Conditions causing hypercalcemia include sarcoidosis, hyperparathyroidism, hypervitaminosis D and cancer.

Calcium supplementation is contraindicated in those hypersensitive to any component of a calcium-containing supplement.

PRECAUTIONS

Supplemental calcium taken without food may increase the risk of kidney stones in women and possibly also in men. It is thought that taking supplemental calcium without food limits the opportunity for the beneficial effect that calcium may have in binding oxalate in the intestine. Therefore, it is advisable that supplemental calcium be taken with food.

Those who form calcium-containing kidney stones are generally advised not to take supplemental calcium.

Those with achlorhydria should take calcium carbonate with food.

ADVERSE REACTIONS

Calcium supplements are generally well tolerated. Use of calcium carbonate may cause such gastrointestinal side reactions as constipation, bloating, gas and flatulence. Prolonged use of large doses of calcium carbonate—greater than 12 grams daily (about 5 grams of elemental calcium)—may lead to the milk-alkali syndrome, nephrocalcinosis and renal insufficiency.

INTERACTIONS

DRUGS

Biphosphonates (alendronate, etidronate, risedronate): Concomitant intake of a bisphosphonate and calcium may decrease the absorption of the bisphosphonate.

H_2 *blockers (cimetidine, famotidine, mizatidine, ranitidine):* Concomitant use of H_2 blockers and calcium carbonate or calcium phosphate can cause decreased absorption of these calcium salts.

Levothyroxine: Concomitant intake of levothyroxine and calcium carbonate was found to reduce levothyroxine absorption and to increase serum thyrotropin levels. Levothyroxine may adsorb to calcium carbonate in an acidic environment, which may block its absorption. There is no evidence that other forms of calcium block levothyroxine absorption if taken concomitantly.

Proton Pump Inhibitors (lansoprazole, omeprazole, rabeprazole sodium): Concomitant use of proton pump inhibitors and calcium carbonate or calcium phosphate can cause decreased absorption of these calcium salts.

Quinolones (ciprofloxacin, gatifloxacin, levofloxacin, lomefloxacin, moxifloxacin, norfloxacin, ofloxacin, sparfloxacin, trovafloxacin): Concomitant use of a quinolone and calcium may decrease the absorption of the quinolone.

Tetracyclines (doxycycline, minocycline, tetracycline): Concomitant intake of a tetracycline and calcium may decrease the absorption of the tetracycline. Tetracyclines may form nonabsorbable complexes with calcium.

Vitamin D Analogues (calcitriol, alfacalcidol): Concomitant use of these vitamin D analogues and calcium can cause increased absorption of calcium.

NUTRITIONAL SUPPLEMENTS

Inositol Hexaphosphate: Concomitant use of inositol hexaphosphate (phytic acid) and calcium may decrease the absorption of calcium.

Minerals (iron, fluoride, magnesium, phosphorous): Concomitant use of iron and calcium may inhibit the absorption of iron. Similarly, concomitant use of fluoride, magnesium, phosphorous or zinc and calcium may decrease the absorption of these minerals. However, these possible mineral interactions have not been shown to be of clinical significance.

Non-digestible oligosaccharides (fructo-oligosaccharides, inulin): Concomitant use of these oligosaccharides and calcium may increase the absorption of calcium in the colon.

Sodium Alginate: Concomitant intake of sodium alginate and calcium may decrease the absorption of calcium.

Vitamin D: Concomitant use of vitamin D and calcium may increase the absorption of calcium.

FOODS

Calcium may be poorly absorbed from foods rich in oxalic acid (spinach, sweet potatoes, rhubarb and beans) or phytic acid (unleavened bread, raw beans, seeds, nuts and grains and soy isolates). Concomitant intake of a calcium supplement with foods rich in oxalic acid or phytic acid may decrease the absorption of calcium. The phytate associated with dietary fiber appears to be the major factor involved in depressing absorption of calcium.

OVERDOSAGE

Overdosage has not been reported with calcium supplements.

DOSAGE AND ADMINISTRATION

There are several different calcium salts available as supplements. These include calcium carbonate, calcium citrate, calcium phosphate, calcium lactate and calcium gluconate. Calcium carbonate and calcium phosphate contain approximately 40% elemental calcium; calcium citrate, approximately 21% elemental calcium; calcium lactate, approximately 13% elemental calcium; calcium gluconate, approximately 9% elemental calcium. Some calcium preparations also contain vitamin D.

Adequate intake of calcium for women and men 19 through 50 years is 1,000 milligrams daily. Adequate intake of calcium for men and women 31 years through greater than 70 years is 1,200 milligrams daily. Adequate intake of vitamin D for women and men 19 to 50 years is 200 IU or 5.0 micrograms daily. Adequate intake of vitamin D for men and women 51 through 70 years is 400 IU or 10 micrograms daily. Adequate intake of vitamin D for men and women over 70 years is 600 IU or 15 picograms daily.

Absorption of calcium is greatest in doses of 500 milligrams or less and when taken with food.

There are several food products, including orange juice, that are now available which have added calcium. The salt calcium citrate malate is used to fortify some foods. Some physicians recommend 1,000 milligrams of supplement calcium daily for postmenopausal women taking estrogen replacement therapy (ERT) and 1,500 milligrams daily for postmenopausal women not taking ERT. An intake of 1,200 milligrams daily appears to be adequate for both groups. The Food and Nutrition Board of the Institute of Medicine of the U.S. National Academy of Sciences has recommended the following adequate intakes (AI) for calcium:

	(AI)
Infants	
0-6 months	210 mg/day
7-12 months	270 mg/day
Children	
1-3 years	500 mg/day
4-8 years	800 mg/day
Boys	
9-13 years	1,300 mg/day
14-18 years	1,300 mg/day
Girls	
9-13 years	1,300 mg/day
14-18 years	1,300 mg/day
Men	
19-30 years	1,000 mg/day
31-50 years	1,000 mg/day
51-70 years	1,200 mg/day
>70 years	1,200 mg/day
Women	
19-30 years	1,000 mg/day
31-50 years	1,000 mg/day
51-70 years	1,200 mg/day
>70 years	1,200 mg/day
Pregnancy	
14-18 years	1,300 mg/day
19-30 years	1,000 mg/day
31-50 years	1,000 mg/day
Lactation	
14-18 years	1,300 mg/day
19-30 years	1,000 mg/day
31-50 years	1,000 mg/day

A LOAEL (lowest-observed-adverse-effect level) in the range of 4 to 5 grams can be identified for adults. Based on this LOAEL and an uncertainty factor (UF) of 2 the Food and Nutrition Board of the Institute of Medicine has recommended the following tolerable upper intake levels (UL) for calcium:

	(UL)
Infants	
0-12 months	Not determinable
Children	
1-18 years	2,500 mg/day
Adults	
19-70 years	2,500 mg/day
>70 years	2,500 mg/day
Pregnancy	
14-50 years	2,500 mg/day
Lactation	
14-50 years	2,500 mg/day

The DV (Daily Value) for calcium, which is used for determining percentage of nutrient daily values on nutritional supplement and food labels, is 1,000 mg. The basis for the DV for calcium is the 1973 U.S. RDA.

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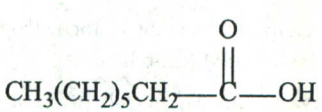
Caprylic Acid

DESCRIPTION

Caprylic acid is a medium-chain 8-carbon saturated fatty acid. It is also known as octanoic acid. It occurs naturally in butterfat and palm and coconut oils in the form of triacylglcerols (TAG). It is represented by the following chemical structure:



Caprylic acid

ACTIONS AND PHARMACOLOGY

ACTIONS

Caprylic acid was reported many years ago to have some antifungal activity *in vitro*. Other *in vitro* studies showed some activity against some viruses and bacteria. The monoglyceride of caprylic acid, monooctanin, given as an infusion into the bile duct, has been used for gallstone dissolution.

MECHANISM OF ACTION

The mechanism of caprylic acid's possible actions is unclear. Caprylic acid may affect the fluidity of viral and fungal cell membranes.

PHARMACOKINETICS

Caprylic acid is absorbed from the intestine and, in contrast with long-chain fatty acids, immediately enters into the portal circulation. It is carried by blood lipids. Most ingested caprylic acid undergoes beta-oxidation in the liver.

INDICATIONS AND USAGE

There is no significant clinical evidence to support an indication for the use of caprylic acid in the treatment or prevention of fungal infections such as *Candida albicans.*

RESEARCH SUMMARY

Some rather old studies reported antifungal activity of caprylic acid *in vitro.* However, clinical use of caprylic acid has not proved to be effective against *Candida albicans* or any other fungi. This is most likely due to the fact that caprylic acid is rapidly metabolized in the usual fatty acid pathways.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to a caprylic acid-containing product.

PRECAUTIONS

Infants, children, pregnant women, nursing mothers and those prone to stomach upsets should avoid caprylic acid supplementation.

ADVERSE REACTIONS

Caprylic acid has an unpleasant rancid taste and may cause mild gastrointestinal symptoms such as nausea and diarrhea.

DOSAGE AND ADMINISTRATION

The usual doses that are taken orally are 300 to 1200 milligrams daily.

LITERATURE

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