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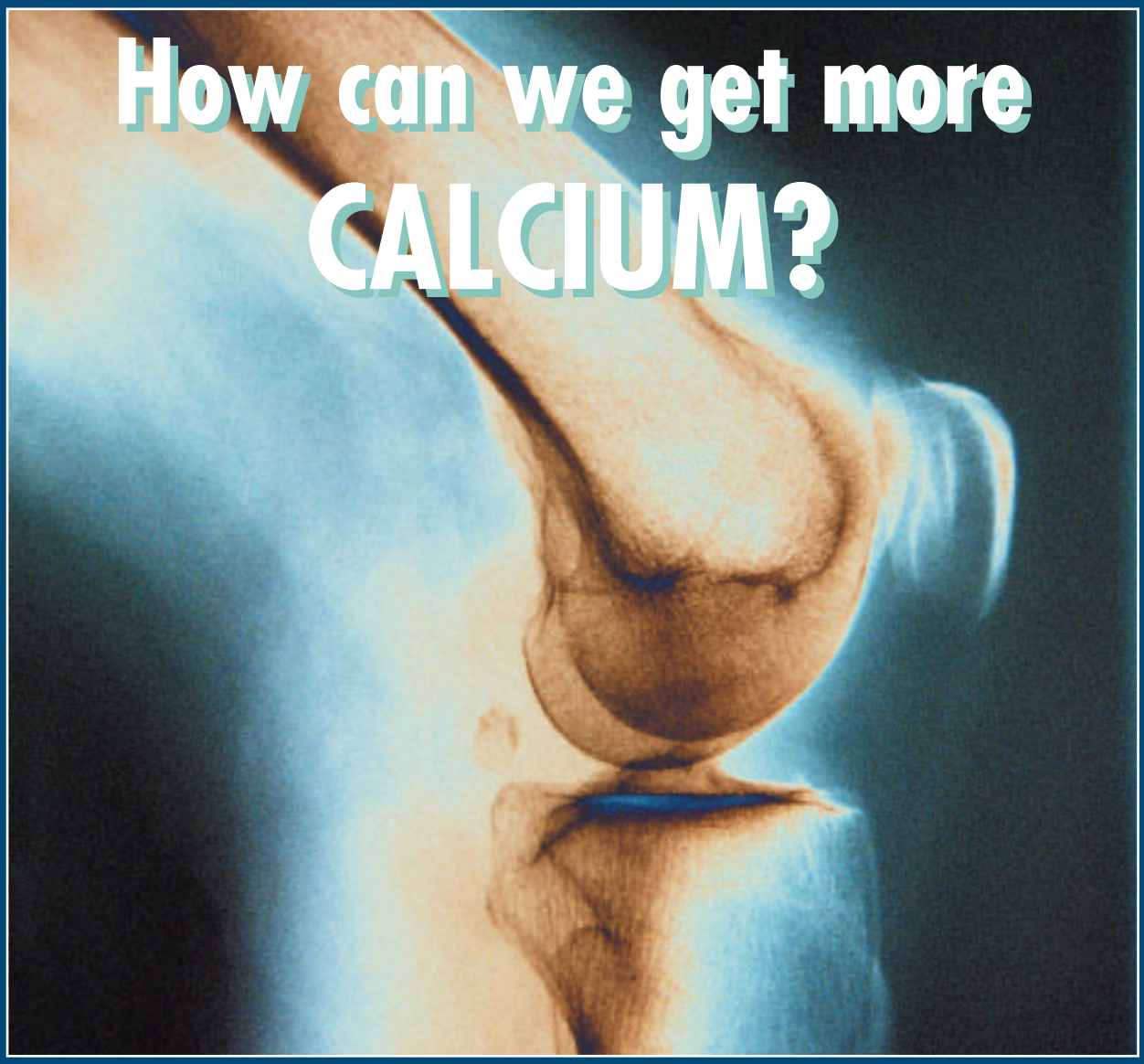
INTERNATIONAL FOOD INGREDIENTS



The analysis of human bones from our mammoth-hunting ancestors show that the primitive food kept their skeletons healthier than our diet today. How can we get more calcium? DR GERHARD GERSTNER, Jungbunzlauer Ladenburg GmbH, focuses on absorption aspects of the readily bioavailable calcium lactate gluconate, which is increasingly used for calcium fortification of foods and beverages

How can we get more

Tricalcium citrate (TCC), calcium lactate, calcium gluconate and calcium lactate gluconate (CLG), a mixture of calcium lactate and calcium gluconate, are organic calcium compounds often used in calcium supplements and calcium fortified foods. As shown in Table 1, their taste is mostly neutral and they offer a good combination between a high calcium content and moderate calcium solubility (TCC) or between a moderate calcium content and a good solubility (calcium lactate, calcium gluconate) or a very high solubility (CLG),

The six to eleven-fold higher solubility of CLG compared to calcium lactate and calcium gluconate results from the fact that CLG is not simply the 'sum' of both salts, but consists of calcium-, lactate- and gluconate-ions and of calcium^{2+}-ions complexed by lactate and gluconate in a specific, pH- and concentration-dependent equilibrium.

The absorption of dietary calcium may in part be determined by the balance between calcium ions (Ca^{2+}), calcium complexes and insoluble calcium salt in the diet, or by the formation of these species in the intestinal lumen. It is often assumed, that calcium is absorbed only in the form of dissolved Ca^{2+}. It has been shown by measuring bi-directional calcium fluxes *in vitro* across segments of the intestine[1] that indeed calcium is absorbed preferentially in its ionic form, while calcium complexes are absorbed intestinally to a lesser degree.

Heaney *et al*[2] also found that solubility and absorbability of different calcium compounds are not linked proportionally with each other, however extreme differences in solubility of calcium compounds do play a role with regard to absorption levels.

DISSOLUTION OF CLG

Besides solubility the dissolution speed of a calcium salt is of certain importance to its bioavailability, at least when calcium bioavailability is estimated through a single measurement of the postprandial calcium concentration peak in serum or urine.

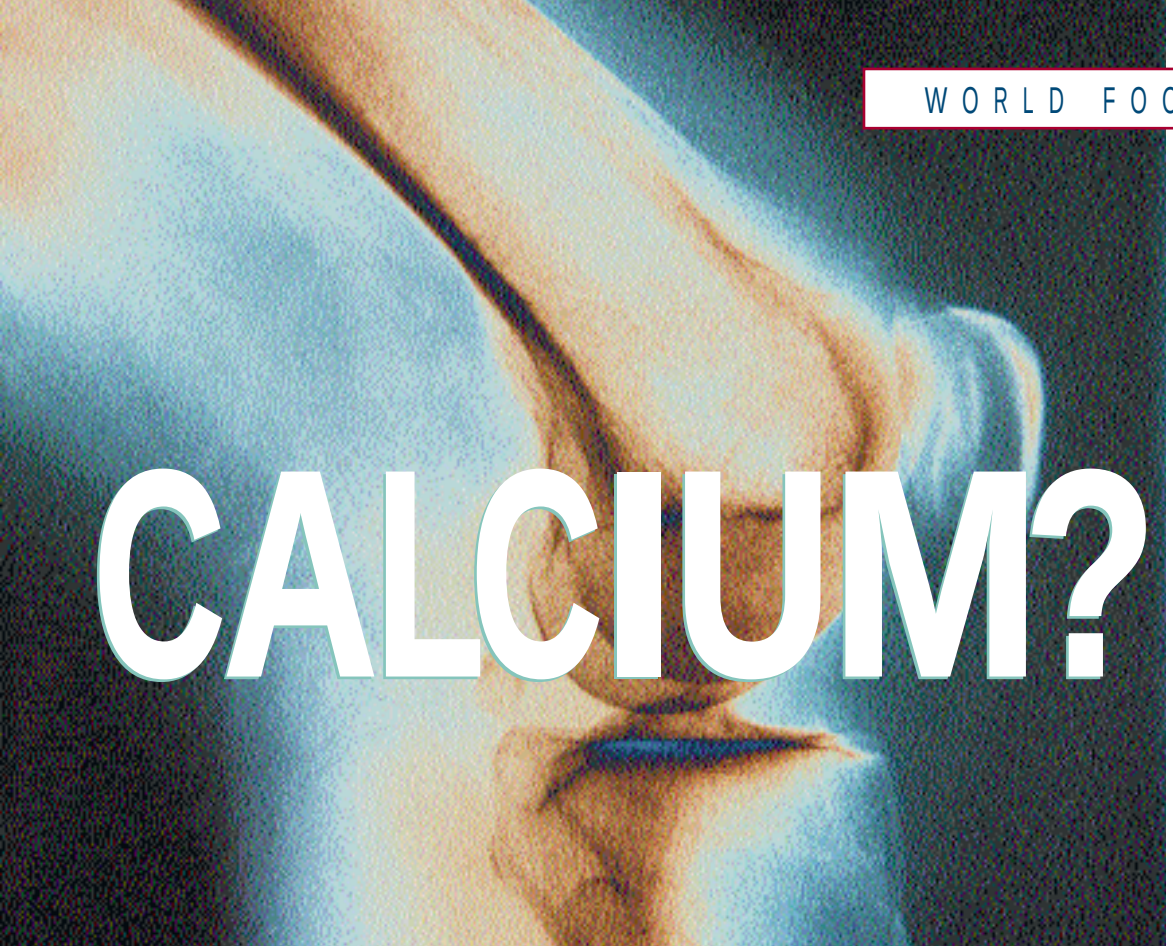
Measuring the dissolution velocity of different calcium preparations, Arteaga *et al*[3] found that among powders and effervescent preparations CLG and TCC had the better dissolution velocities *in vitro*, that were independent of pH (95-105% of both salts were dissolved within 60 min at room temperature).The dissolution velocity of several calcium carbonate preparations ranged from negligible 0.7±0.8% under conditions of achlorhydria (pH 6.9) to 77.2±17.5% at pH 1.5. Solubility of complex-forming soluble organic salts as CLG or TCC is largely pH-independent[3]. Therefore, complex-forming soluble organic salts such as CLG or TCC are better suited than calcium carbonate for achlorhydric subjects or elderly people of whom gastric acid production is frequently decreased.

CALCIUM ABSORPTION OF CLG

The fractional absorption rate of calcium from well absorbable soluble calcium salts and from milk ranges between 25 and 33% in healthy subjects. Werner *et al*[4] compared true calcium absorption from CLG and

TABLE 1. PROPERTIES OF CLG COMPARED TO OTHER COMMONLY USED SOLUBLE ORGANIC CALCIUM SALTS IN WATER

Product	Calcium content	Solubility [g/L water]	Solubility [g Ca/L water]	Taste
Calcium lactate gluconate	13%	400	52	Neutral
Calcium lactate	13%	66	9	Bitter at higher concentrations
Calcium gluconate	9%	35	3	Neutral
Calcium citrate	21%	1	0.2	Neutral



Calcium intake is not sufficient in our society - drawing more attention to the bioavailability of the calcium in our diet

foods, applying a highly precise double isotope technique. Eight healthy subjects (44-58 years) ingested in randomised order a CLG effervescent tablet (containing 500 mg Ca), milk (620 mg Ca) or a breakfast (equal to 580 mg calcium). All test preparations were labelled with ^{44}Ca and given on an empty stomach, whereas ^{42}Ca was injected intravenously. Corresponding to the high solubility of CLG, fractional true calcium absorption from CLG (28.7±9.1%) was higher than from milk (24.0±5.4) or the meal (17.9±7.1).

However, the majority of investigations in true or apparent calcium absorption from CLG or in metabolic responses to supplementary calcium loads did not use the pure salt but a mixture of CLG with calcium carbonate (CLG+C). Addition of calcium carbonate to CLG reduces tablet size mainly due to the higher calcium content of the carbonate salt. Therefore, CLG supplements currently prescribed by physicians often contain calcium carbonate (ie Calcium Sandoz Forte). Calcium absorption from such a mixture however may be lower than from pure CLG, possibly because the concentration of calcium lactate and gluconate in CLG+C is lower compared to CLG. Unfortunately, there is no published clinical trial comparing CLG+C directly with pure CLG.

In a study by Behne *et al*[5], two doses CLG+C, equivalent to 500 or 1000 mg calcium, were administered orally to eight healthy young adults (22-32 years), and calcium absorption was determined applying a double isotope method. Irrespective of the Calcium dose, absorption was about 30%, being on the same level as CLG alone.

In all the other studies, in which calcium absorption was measured either applying double isotope techniques or by faecal excretion or whole body retention of a single calcium isotope, minimum values of fractional calcium absorption from CLG+C lay between 17 and 26%. This was equal to or less than the absorption of calcium carbonate (20% or 22.8-25.6%, respectively) in studies of Berstad[6] and Ekman[7], less than absorption from a TCC solution (29.3%) but comparable with a suspension of TCC (25%)[8].

EFFECTS OF CLG ON IONISED CALCIUM AND PTH

Several investigations in bioavailability of CLG made use of biomarkers instead of measuring calcium absorption directly. Preferred markers are the postprandial calcaemic and calciuric response to and the decrease in serum parathyroid hormone (PTH) levels following oral administration of calcium supplements or calcium-rich foodstuffs.

Comparing the postload serum calcium and PTH-response following administration of 400 mg calcium to nine healthy female volunteers (24-34 years) either as CLG+C or in Emmentaler cheese (considered as a very good source of dietary calcium), milk, spinach and sesame seed, Kärkkäinen *et al*[9] found, that CLG+C induced a higher increase in serum ionised calcium than cheese, milk, vegetable foodstuffs or the control and a significant greater decline in serum intact PTH than milk, spinach or sesame seed.

A significant increase in urinary calcium excretion was observed following CLG+C, milk and cheese , but not after spinach or sesame seed. These data give indication of a comparable high calcium bioavailability from CLG+C and Emmentaler cheese, which is better than that from milk and much better than cal- ▶

TABLE 2: EFFECTS OF CALCIUM (CA) SUPPLEMENTATION WITHOUT ADDITIONAL VITAMIN D ON BONE MINERAL DENSITY (BMD) OF THE LUMBAR SPINE. CHANGES ARE PRESENTED AS A PERCENTAGE FROM BASELINE AFTER 12-48 MONTH OF INTERVENTION[19]

Age	Ca supplemented per day	Ca diet	%Increase in BMD[1] from	Reference
			CLG+C	
68 y	1000mg	990 mg	+1.8	20
58 y	1000mg	760 mg	+0.2	21
58 y	1000mg	700 mg	+0.8	22
62 y	1000mg	820 mg	+0.2	23
64 y	1000mg	NR	+0.8	24
70 y	500mg	NR	+1.0	25
65 y	500mg	NR	+1.5 to +1.8	26
			Ca Citrate	
66 y	1250mg	700 mg	+2 - +2,8	27
63 y	500mg	875 mg	-0.8 to -0.1	28
			Ca Citrate Malate	
60 y	500mg	400 mg	-1.0 to -0.3	29
			Ca Carbonate	
63 y	500mg	NR	-0.4 to +0.4	30
64 y	500mg	NR	-0.5	31
60 y	500mg	400 mg	-0.3 to -2.0	29

1lumbar spine; NR = not recorded

INFORMATION

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◀ cium bioavailability of vegetable sources like spinach or sesame seed.

Other clinical studies in the metabolic response (i.e. PTH and urinary and serum ionised Ca^{2+}) to 500 or 1000 mg calcium in the form of CLG, CLG+C or other Ca-supplements are hardly to compare with each other and do not allow a ranking of different calcium sources. Altogether they show a high absorbability or bioavailability, respectively, of calcium from CLG or CLG+C[10-16].

IMPROVING BONE HEALTH WITH CLG

The main purpose of the recommended high calcium intake is osteoporosis prevention. Therefore an increase in bone mineral density (BMD) or bone stability is a better criterion for the efficacy of a calcium salt than its absorbability.

CLG, when administered to 19 nonmenopausal women with osteoporosis during or after a hormone therapy, significantly reduced bone fracture rate[17]. Moreover, in a study in 50 Chinese women, aged 62-92, CLG increased BMD of the hip more than exercise[18].

Additional evidence of beneficial effects on bone health of CLG+C was supplied by a meta-analysis of Schaafsma *et al*[19]. The authors compared 16 clinical studies in elderly and late postmenopausal women (mean age 58-79 years), who were supplemented for 12-48 month with 500-1250 mg/d calcium as CLG+C, Ca carbonate, Ca citrate, and other salts. Without exception, intake of CLG+C increased BMD of the lumbar spine by + 0.2 to +1.8%, whereas other supplements, even very well absorbable salts as Ca citrate malate, partly decreased BMD (Table 2).

CONCLUSION

CLG has the benefit to be among the most soluble calcium salts used for calcium supplementation, displaying a rapid rate of dissolution, a high stability and also a neutral taste, even at higher concentrations. Further to its excellent solubility, it is well absorbed and shows a high bioavailability in human studies (up to 30 %), which is equal or even superior to calcium bioavailability of milk.

Most available studies did not evaluate CLG alone, but rather the combined supplement CLG + calcium carbonate. A recent meta-analysis of this combination and other calcium sources revealed that it was both significantly and more consistently able to increase bone mineral density of the lumbar spine in elderly women. This effect may even be more pronounced when CLG is applied without calcium carbonate.

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