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How can we get more CALCIUM?

Jungbunzlauer

presents

An exclusive report on calcium lactate gluconate bioavailability
Ca, ricalcium 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-square-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 (Ca²⁺), 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 Ca²⁺. It has been shown by measuring bi-directional calcium fluxes in vitro across segments of the intestine that indeed calcium is absorbed preferentially in its ionic form, while calcium complexes are absorbed intestinally to a lesser degree.

Heaney et al. 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. 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. 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. compared true calcium absorption from CLG and tricalcium citrate (TCC), calcium lactate, 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).

<table>
<thead>
<tr>
<th>Product</th>
<th>Calcium content</th>
<th>Solubility [g/L water]</th>
<th>Solubility [g Ca/L water]</th>
<th>Taste</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium lactate gluconate</td>
<td>13%</td>
<td>400</td>
<td>32</td>
<td>Neutral</td>
</tr>
<tr>
<td>Calcium lactate</td>
<td>13%</td>
<td>66</td>
<td>9</td>
<td>Better at higher concentrations</td>
</tr>
<tr>
<td>Calcium gluconate</td>
<td>9%</td>
<td>35</td>
<td>3</td>
<td>Neutral</td>
</tr>
<tr>
<td>Calcium citrate</td>
<td>21%</td>
<td>1</td>
<td>0.2</td>
<td>Neutral</td>
</tr>
</tbody>
</table>
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 44Ca and given on an empty stomach, whereas 42Ca 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, 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 and Ekman, less than absorption from a TCC solution (29.3%) but comparable with a suspension of TCC (25%).

Calcium intake is not sufficient in our society - drawing more attention to the bioavailability of the calcium in our diet.
PERCENTAGE FROM BASELINE AFTER 12-48 MONTH OF INTERVENTION

<table>
<thead>
<tr>
<th>Age</th>
<th>Ca supplemented per day</th>
<th>Ca diet</th>
<th>% Increase in BMD</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>68 y</td>
<td>1000mg</td>
<td>990 mg</td>
<td>+1.8</td>
<td>20</td>
</tr>
<tr>
<td>58 y</td>
<td>1000mg</td>
<td>760 mg</td>
<td>+0.2</td>
<td>21</td>
</tr>
<tr>
<td>58 y</td>
<td>1000mg</td>
<td>700 mg</td>
<td>+0.8</td>
<td>22</td>
</tr>
<tr>
<td>62 y</td>
<td>1000mg</td>
<td>820 mg</td>
<td>+0.2</td>
<td>23</td>
</tr>
<tr>
<td>64 y</td>
<td>1000mg</td>
<td>NR</td>
<td>+0.8</td>
<td>24</td>
</tr>
<tr>
<td>70 y</td>
<td>500mg</td>
<td>NR</td>
<td>+1.0</td>
<td>25</td>
</tr>
<tr>
<td>65 y</td>
<td>500mg</td>
<td>NR</td>
<td>+1.5 to +1.8</td>
<td>26</td>
</tr>
<tr>
<td>66 y</td>
<td>1250mg</td>
<td>700 mg</td>
<td>+2.0 to +2.8</td>
<td>27</td>
</tr>
<tr>
<td>63 y</td>
<td>500mg</td>
<td>875 mg</td>
<td>−0.8 to −0.1</td>
<td>28</td>
</tr>
<tr>
<td>60 y</td>
<td>500mg</td>
<td>400 mg</td>
<td>−1.0 to −0.3</td>
<td>29</td>
</tr>
<tr>
<td>63 y</td>
<td>500mg</td>
<td>NR</td>
<td>−0.4 to +0.4</td>
<td>30</td>
</tr>
<tr>
<td>64 y</td>
<td>500mg</td>
<td>NR</td>
<td>−0.5</td>
<td>31</td>
</tr>
<tr>
<td>60 y</td>
<td>500mg</td>
<td>400 mg</td>
<td>−0.3 to −2.0</td>
<td>29</td>
</tr>
</tbody>
</table>

1 lumbar spine; NR = not recorded

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\(^1\). Moreover, in a study in 50 Chinese women, aged 62-92, CLG increased BMD of the hip more than exercise\(^2\).

Additional evidence of beneficial effects on bone health of CLG+C was supplied by a meta-analysis of Schaafsma et al.\(^3\). 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.

REFERENCES