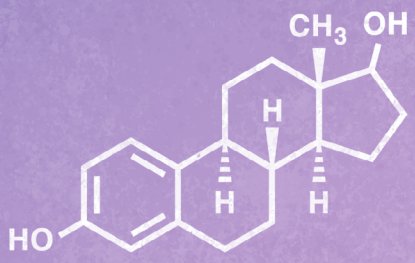
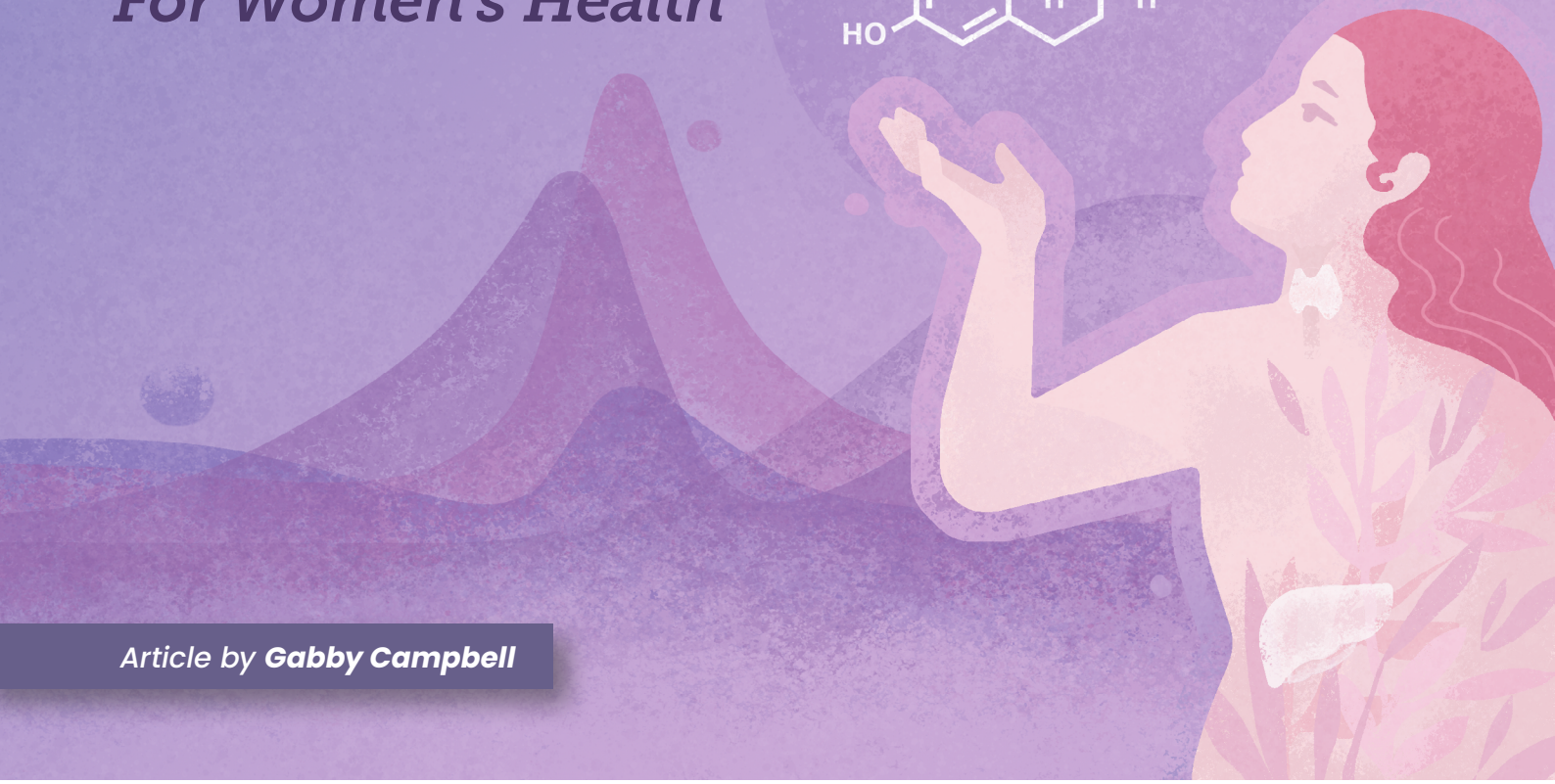
Calcium

For Women's Health





Article by ***Gabby Campbell***

Known for its important role in skeletal health and the prevention of osteoporosis, a reduced dietary calcium intake and an increased physiological need can have a profound effect on the individual beyond bone health. In this article, we review the functions of calcium within the body and look at dietary and supplemental sources of calcium. We take a closer look at the rationale for supplementation across the lifespan and showcase the role of calcium D-glucarate supplementation, looking at its unique role in hormone regulation.

Calcium is an essential macronutrient found in abundance in the body, with 99% stored in teeth and bone.[1] This mineral is involved in several biochemical processes, including:

- Hormonal secretion
- Nerve impulse transmission
- Muscular function
- Vascular contraction
- Vasodilation
- Intracellular signalling. [1,2]

Lifespan calcium requirements

Calcium plays an important role in women's health, with intake requirements differing across the lifespan.

Higher doses of calcium are required during pregnancy and breastfeeding[3] to:

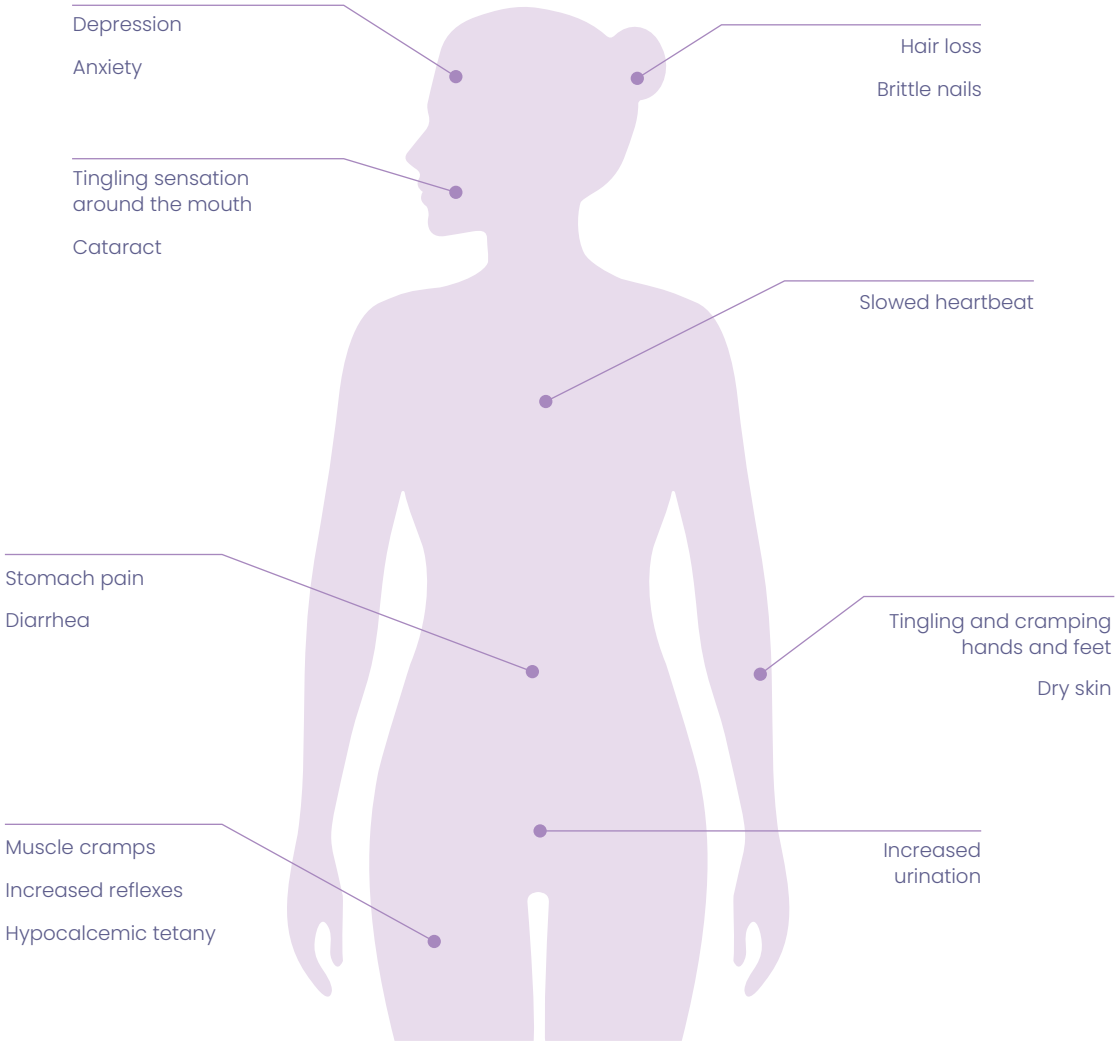
- Minimise bone mineral loss
- Aid skeletal growth of the child[4]
- Support milk production[4]
- Prevent pre-eclampsia.[3]

Higher doses are also needed for menopausal and post-menopausal women, as the drop in oestrogen necessary for bone formation causes more bone resorption, increasing the risk of osteoporosis and osteoporotic fractures.[5]

Calcium deficiency

With the wide-ranging role of calcium throughout the body, Fig. 1 depicts some of the physical expressions of calcium deficiency.

Fig. 1. Signs of calcium deficiency.



Calcium in the diet

Meeting the requirements for calcium can be challenging - 1 in 10 Australians do not meet their daily calcium requirements through diet.[6] While dietary intake of calcium in childhood is generally sufficient, intake drops during adolescence in Australia.[7] A staggering 90 per cent of women between the ages of 12-18 years and over 50 years were found to have insufficient dietary calcium in Australia, despite an increased need.[6] The number of Australians choosing to avoid animal products and switching to plant-based alternatives is increasing and while plant-based milk and dairy alternatives provide a dairy replacement from a taste perspective, unless they are fortified with calcium, they often do not provide the calcium benefits of dairy products.[7]

Generally, dietary intake of calcium is sufficient for most people, provided their diet contains no restrictions. There are, however, some individuals who may benefit from supplementation including individuals who:

- Take corticosteroids
- Diagnosed with osteopenia or osteoporosis
- Follow a vegan or dairy-free diet or those with a lactose intolerance
- Women with amenorrhea
- Residents of aged / long-term care facilities
- Individuals with gastrointestinal (GI) diseases, given dietary calcium is largely absorbed in the small intestine.[2,8]

Supplemental calcium

The two most common forms of supplemental calcium include calcium carbonate and calcium citrate, followed by calcium hydroxyapatite. Several factors for consideration when prescribing are outlined in the table below (See Tables 1 and 2). Regardless of the form chosen, **absorption is best when taken with food, in divided doses of 500mg or less at a time and when given concurrently with vitamin D.**[9]

Table 1. Analysis of supplemental forms of calcium.

Form of calcium	*Considerations*
Calcium carbonate	Generally well absorbed and tolerated when taken with food, though best avoided by those taking H2 blockers or proton pump inhibitors (PPIs), or individuals with hypochlorhydria as it requires an acidic environment for optimal absorption. Provides a higher amount of elemental calcium per tablet, so is best for cost and compliance considerations,[9] however, is also the form most associated with GI disturbance.[2]
Calcium citrate	Best absorbed and most bioavailable form of calcium when taken with food. It can also be taken without food if needed with little to no GI disturbance. The best form for patients on PPIs or H2 blockers, those with hypochlorhydria, inflammatory bowel disease or other GI absorption disorders.[9]
Calcium phosphate / Calcium hydroxyapatite	Aids bone and mineral regeneration, helps maintain strong bones and can also lessen the risk of osteoporosis.[10] Several studies have shown this form aids improvement in blood lipid profile, GI hormone secretion, microbial composition of the gut, and increases bile acid secretion.[9]
Calcium lactate and Calcium gluconate	Much less concentrated forms of calcium requiring high dosing, which is expensive and impractical for patients.[11]

Table 2. Calcium supplementation recommended dosage.

Concern	*Dosage*
General dietary or total calcium needs for women.	1,000 mg/day[12]
GI diseases such as coeliac disease.	1,200 - 1,500 mg/day plus 1000 IU vitamin D per day[13]
Menopausal and post-menopausal women over 50 years, for the reduction of osteoporosis and osteoporotic fractures.	1,000 – 1,200 mg/day plus 400 IU – 800 IU vitamin D per day[2,14]
Pregnancy and lactation.	1,500 – 2,000 mg/day[3]
Women with amenorrhoea.	1,200-1,500 mg/day plus 400-1000 IU vitamin D per day[15]
If taking certain medications (e.g. Corticosteroids).	1200 mg/day plus 800 – 2000 IU vitamin D per day[16]

Calcium D-Glucarate Liver and Hormone Regulation

Calcium D-glucarate is the calcium salt and supplemental form of D-glucaric acid, an endogenously produced compound. Calcium's function is to stabilise glucaric acid, not act as a calcium supplement – glucaric acid is the active ingredient in the supplement.

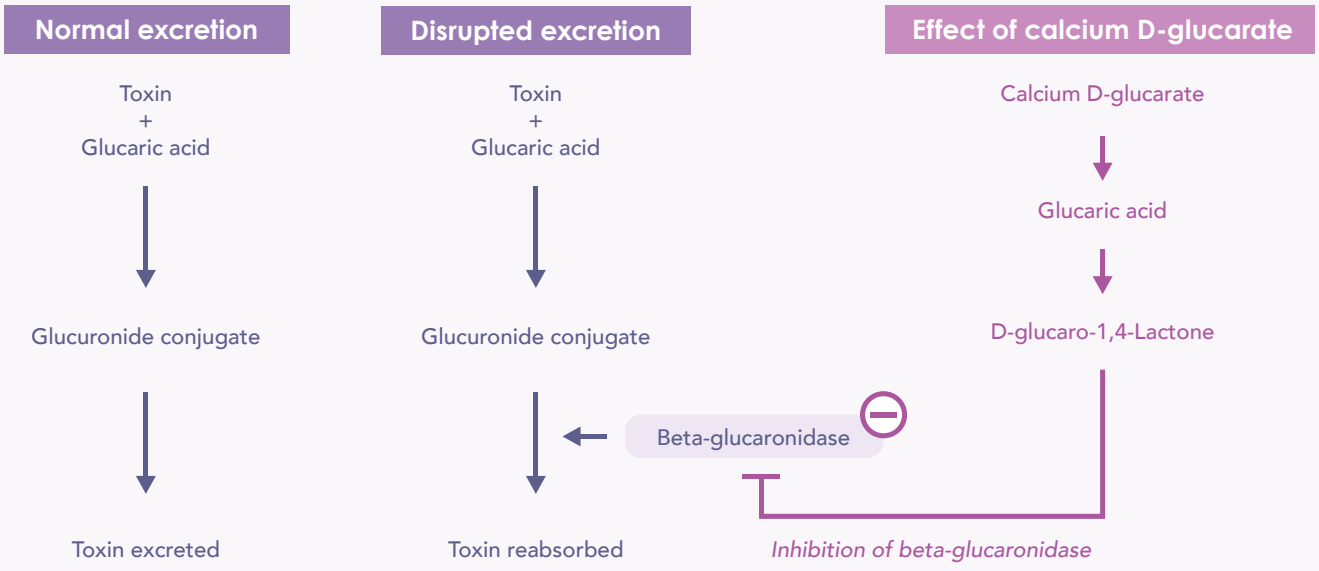
When ingested, calcium D-glucarate liberates D-glucaric acid which is further metabolised into D-glucaro-1,4-lactone or D-glucaro-6,3-lactone known for their beneficial role in liver support, lipid and hormonal regulation, including oestrogen metabolism.[17] Glucaric acid's primary action is through the inhibition of beta-glucuronidase – a specialised enzyme produced by colonic gut microbiota involved in the interference of phase II liver detoxification - glucuronidation. (See Fig. 2)[17]

Glucuronidation

Glucuronidation is the detoxification process performed by the liver, responsible for the detoxification and elimination of hormones and exogenous toxins. (See Fig. 2) The process of glucuronidation involves the binding of glucuronic acid to form glucuronide conjugates with toxins, in preparation for elimination. Excess beta-glucuronidase has the capacity to deconjugate these compounds, allowing for the reabsorption of toxins. Furthermore, excess beta-glucuronidase is associated with an increased risk for hormone-dependent cancers such as breast, colon, and prostate cancers.[17]

Supplemental calcium D-glucarate may be considered as a treatment strategy in addition to lifestyle and dietary modifications.[17] Current research suggest supplemental doses of calcium D-glucaric acid of 1500-3000 mg/day, with supplementation not recommended during pregnancy due to the role of calcium D-glucarate in hormone detoxification.[17]

Fig. 2. The function of calcium D-glucarate in detoxification. Calcium D-glucarate enhances phase 2 glucuronidation by inhibiting beta-glucuronidase.



Calcium supplementation for specific conditions

Calcium supplementation and cardiovascular disease risk in women

Research on calcium supplementation and cardiovascular disease (CVD) has been divisive, with studies producing contradictory results. In some studies, lower doses of calcium supplementation (600 mg/day) decreased CVD risks,[2] while others demonstrate a considerable increase with doses of 700–1000 mg/day.[18] The assumption being that increased calcium may contribute to raised serum calcium levels potentially hastening coronary artery calcification.[2] With no conclusive outcome, and generally favourable results on CVD in the literature, calcium supplementation is still believed to be beneficial overall.[2]

Calcium supplementation, osteoporosis and falls risk in women

Calcium requirements increase for women during and post menopause, as reduced levels of oestrogen precipitate a decrease in the absorption and preservation of calcium. This reduction of calcium absorption and preservation can affect bone mineral density and lead to osteoporosis. When combined with weakened muscles, curvature of the spine or poor postural control experienced with ageing, these women tend to also have a higher risk of falls and fracture.[19] Research supports supplementing with both calcium and vitamin D, as a deficiency can further inhibit calcium absorption in older women to positively impact calcium homeostasis, mitigating these concerns.[7,20]

Calcium supplement for pre-eclampsia prevention during pregnancy

Pre-eclampsia is a complication that can occur in pregnancy and commonly affects 2-5% of pregnant women. It is a multisystem condition characterised by hypertension (≥140 mmHg/≥90 mmHg) and proteinuria (≥300 mg/day) typically presenting after 20 weeks' gestation. Other symptoms may include neurological and haematological complications, in addition to liver abnormalities and acute kidney injury.[21,22]

Current research supports calcium supplementation during pregnancy to reduce the risk of pre-eclampsia onset. Doses between 1-2 g/day are considered safe and effective and this is especially important for women with a low dietary intake of calcium, or those with predisposing factors putting them at risk of developing pre-eclampsia.[23, 24]

Kidney stone formation associated with calcium supplementation

Where once the recommendation in the management of kidney stones was dietary calcium restriction,[25] more recent research highlights that a dietary calcium intake greater than 500 mg/day may be protective against the formation of kidney stones by decreasing the absorption of oxalates and reducing urinary oxalate levels.[2] In contrast, supplemental calcium may increase the risk, which could be mitigated by taking the supplement with food, though this is currently speculative.[2]

Gastrointestinal effects and calcium supplementation

GI side effects may occur with high-dose calcium supplementation and are often associated with calcium carbonate.[2] Symptoms are mostly minor and may include an increased prevalence of abdominal pain, bloating, flatulence, severe diarrhoea and constipation.[26] In some instances, adverse effects from larger supplement doses can be severe and may require hospitalisation.[26]

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