

# Calcium Supplementation: Why, Which, and How?

## INTRODUCTION

The word calcium is derived from a Latin word “*calx* or *calcis*” which means “lime.” Calcium was known as early as the 1<sup>st</sup> century when ancient Romans prepared lime as calcium oxide; however, it was isolated in 1808 by Englishman Sir Humphrey Davy. In 1883, Sydney Ringer demonstrated the biological significance of calcium, when he showed that frog hearts needed the presence of calcium in the bathing solution in order to continue beating.

Calcium as a nutrient is most commonly associated with the formation and metabolism of bone. Over 99% of the total body calcium is found as calcium hydroxyapatite ( $\text{Ca}_{10}[\text{PO}_4]_6[\text{OH}]_2$ ) in bones and teeth. The rest 1% is intracellular and about 0.1% is in extracellular fluid. Calcium is an important intracellular and extracellular cation, which is required physiologically for muscle contraction, nerve conduction, vascular reactivity, and hormonal secretion. Calcium in plasma or serum exists in the following three forms or fractions: ionized or free calcium (50%), protein-bound calcium (40%), and complexed or chelated calcium which is bound to phosphate, bicarbonate, sulfate, citrate, and lactate (10%).<sup>[1]</sup>

According to the Institute of Medicine,<sup>[1]</sup> daily allowance for calcium ranges from 600 to 1300 mg in relation to age and gender. The Indian Council of Medical Research<sup>[2]</sup> recommends 600 mg for both genders. In the USA and Northern Europe, the average daily intake of calcium is about 900–1000 mg, and in South Asia and India, it is 400–500 mg.<sup>[3,4]</sup> This means that at both geographical areas, intake of calcium is suboptimal in >50% of population. This also gives impression that these all people require calcium supplementation. If this holds true, then it has huge financial and commercial implications. If more than half of the world’s population is calcium deficient, then why we do not observe its consequences often? To address this question, we first discuss the physiological aspects of calcium homeostasis, then discuss about when, which, and how calcium supplementation should be given.

## PHYSIOLOGY OF CALCIUM HOMEOSTASIS

Calcium is absorbed actively in the duodenum through transcellular (active transport – 80%) process which is Vitamin D dependent, whereas passive absorption is a paracellular (passive diffusion – 20%) process which occurs throughout intestine independent of Vitamin D and is dependent on the concentration of calcium in the intestinal tract. The total fraction of calcium absorbed from the total intake can vary from 20% to 80%. In the event of decreased calcium availability from intake, calcium is released from the bone under the effect of Vitamin D–parathyroid hormone (PTH) system to maintain its

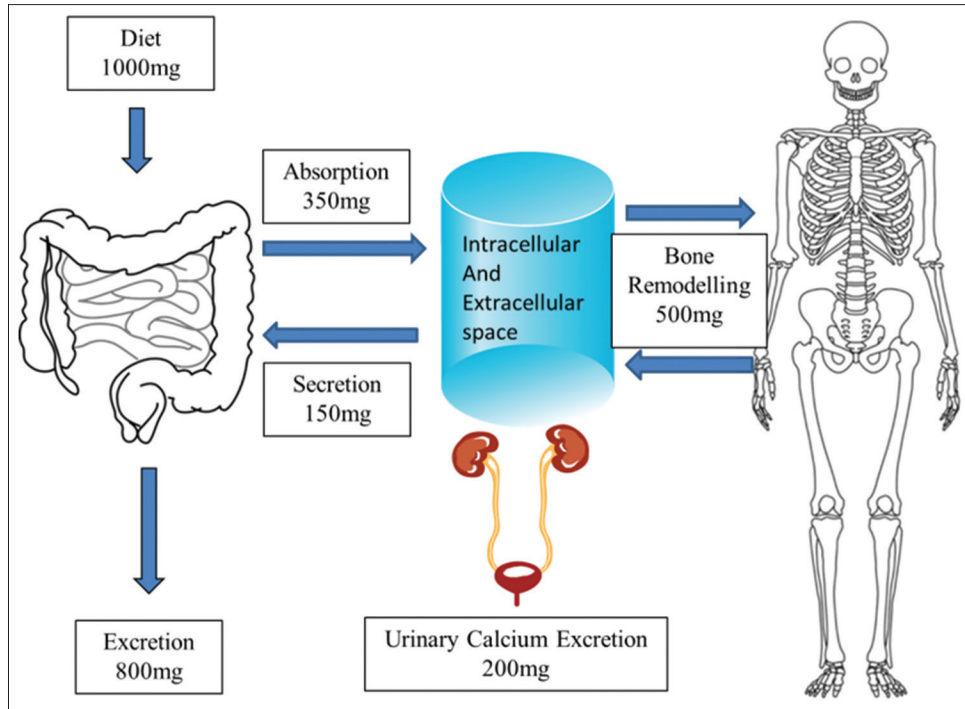
homeostasis. Calcium excretion is also dependent on calcium balance. Normally, about 98% of filtered calcium is absorbed from the kidney and about 150–250 mg is excreted in urine daily, which is compensated by intestinal calcium absorption or bone resorption. Serum calcium is maintained in narrow range with contribution from calcium absorption, bone remodeling, and calcium excretion [Figure 1].<sup>[1]</sup>

## WHY – CALCIUM SUPPLEMENTATION?

“...Something that is added to something else in order to improve it or complete it.”

– Cambridge Dictionary

According to the above-stated recommendations, more than half of the world’s population will require calcium supplementation. Calcium supplementation is decided by recommended daily allowances. Logically, to maintain calcium homeostasis, first, the body will try to absorb maximum available calcium, rather than affecting bone remodeling. Hence, calcium absorption is the first most important adaptive mechanism. It is well known that fractional calcium absorption (FCA) is inversely proportional to the calcium intake. High FCA (54%–63%) has been reported from the region of China with low calcium intake (<500 mg)<sup>[5]</sup> compared to 25%–34% among US children with high intake of calcium (>900 mg).<sup>[6]</sup> There are no such studies reported from India, because this requires double calcium isotopes, which are not available in India. Calcium absorption is mainly facilitated by Vitamin D. The conventional explanation of homeostasis is by systemic adaptation in which decreased calcium intake results in decreased calcium absorption, which leads to increase in PTH levels. The PTH upregulates the 1- $\alpha$  hydroxylase enzyme, leading to increase in the generation of 1,25-dihydroxyvitamin D (1,25(OH)<sub>2</sub>D) levels and increased calcium absorption. However, calcium absorption can be kept static over a wide range of calcium intake and serum 25OHD levels.<sup>[7]</sup> Calcium absorption varies between 20% and 70% at the serum 25OHD levels >10 ng/ml<sup>[8]</sup> and does not increase with higher levels of 25OHD.<sup>[9]</sup> This suggests that it is the calcium absorptive mechanism, rather than dietary calcium intake, will decide the adequacy of calcium homeostasis. An alternative hypothesis has been proposed, wherein the adaptation of calcium absorption occurs at the level of intestine called “intestinal calcistat.”<sup>[10,11]</sup> This “calcistat” senses the calcium intake or available calcium in the gastrointestinal (GI) tract and regulates the generation of active Vitamin D in intestinal cells to adjust FCA. With daily calcium intake of <500 mg, the FCA is about 60%–80%, which can easily supply the daily needs of calcium, i.e., 200 mg. In contrast, with daily calcium intake of >900 mg, FCA is about 25%–35% to maintain calcium homeostasis.



**Figure 1:** Physiology of calcium homeostasis

According to the above discussion, about 400–500 mg of elemental calcium daily should be able to meet daily requirement. The average daily intake of calcium in India ranges from 200 to 600 mg among various studies. This suggests that those with low calcium intake should either increase calcium intake by modifying their diet or take calcium supplements.

### WHICH – DIET VERSUS CALCIUM SUPPLEMENTATION?

The American Association of Clinical Endocrinologists (2016) guideline recommends that calcium intake among adults aged 50 years and older (including diet, plus calcium supplements, if necessary, if dietary intake is insufficient) should be 1200 mg/day.<sup>[12]</sup> The United States Preventive Task Force (USPTF) concludes that the current evidence is insufficient to assess the balance of the benefits and harms of combined Vitamin D and calcium supplementation. It recommends against daily supplementation of more than 1000 mg of calcium.<sup>[13]</sup>

The main sources of calcium are dairy products such as milk, curd, and cheese. Other foods such as grains, legumes, fruits, and vegetables also contribute to calcium intake (Figure 2, National Institute of Nutrition, Hyderabad, at fitjog.com). It will be desirable to increase calcium intake through modification of diet. Daily intake of two glasses of milk or curd with enough pulses can meet the calcium requirement of body without the need for any dietary supplementation.

Many calcium supplements are available in Indian markets [Table 1]. Calcium is available as carbonate, citrate, acetate, phosphate, lactate, and gluconate, with varying concentrations of ionic calcium contents as summarized in Table 1.

**Table 1: Calcium Supplements**

Preparation	Calcium (%)	Calcium (mg/g)
Calcium carbonate (Shelcal)	40	400
Calcium phosphate (Ostocalcium)	38	383
Calcium citrate (Ucal)	21	210
Calcium acetate (Eliphos®)	25	253
Calcium lactate (Decal)	13	130
Calcium gluconate (Calcium Sandoz)	9	93

### HOW – CALCIUM SUPPLEMENTATION?

Calcium carbonate is the least expensive and requires the fewest tablets. However, it may cause constipation and bloating and must be taken with meals for adequate absorption. Calcium citrate is often more expensive than calcium carbonate and requires more tablets to get the desired dose. Its absorption is not dependent on gastric acid, and it is less likely to cause GI side effects. For optimal absorption, the dose of calcium should not exceed 500 mg per dose, irrespective of calcium preparation. For patients requiring >500 mg/day, the dose should be divided.

All nutrients have side effects when taken in excess quantity like obesity with excess calories. There are contradictory evidences about increased calcium intake and cardiovascular deaths both from observational studies and meta-analyses.<sup>[14-16]</sup> Previous studies and meta-analyses found no correlation between calcium intake and cardiovascular mortality. A recently published large prospective observational study among Swedish females found a positive relation between calcium intake and cardiovascular death.<sup>[16]</sup> Increased

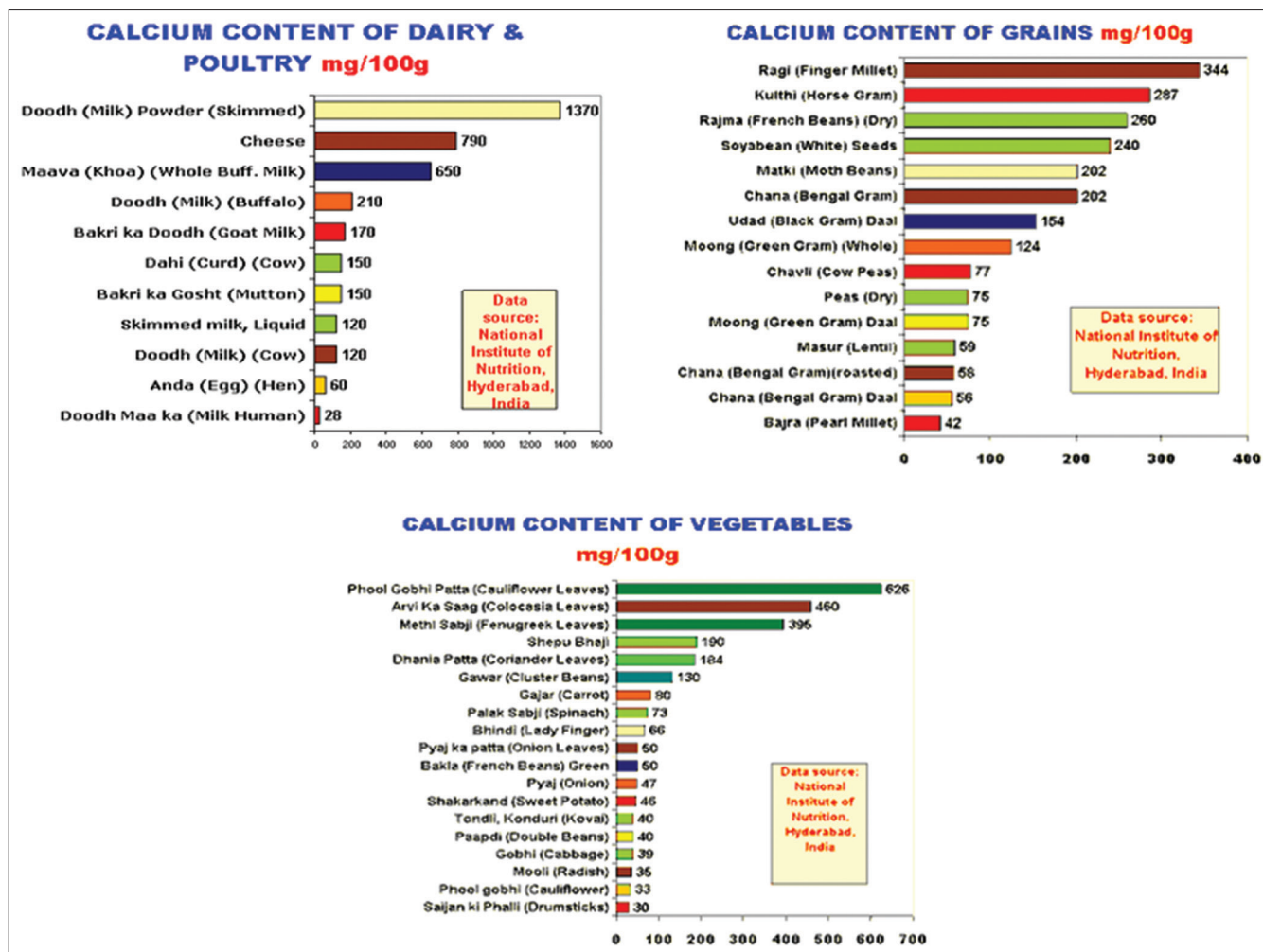


Figure 2: Dietary contents of calcium

serum calcium will suppress PTH and also increase serum levels of fibroblast growth factor 23 which is known to be associated with an increased risk of cardiovascular events and all-cause mortality.<sup>[17]</sup> Increased serum calcium level induces hypercoagulable state and can increase the risk of cardiovascular mortality.<sup>[18]</sup>

Hence, to conclude, we should not be overenthusiastic to prescribe calcium supplementation to all but be cautious. It should be prescribed after due consideration and diligence to those whose dietary calcium intake is insufficient and can be increased by dietary means due to food intolerance or avoidance.

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