REVIEW ARTICLE

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Influential Factors in Intestinal Absorption and Renal Reabsorption of Calcium

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Abstract

Calcium is one of the vital and essential elements in the body, serving as a primary constituent of bones and teeth. It plays a fundamental role in nerve signal transmission, muscle contractions, heart rate regulation, blood clotting, energy production, glandular secretion, and immune system maintenance. Calcium is abundantly found in dietary sources, with most of it residing in the teeth and bones within the body. Approximately 40% of daily dietary calcium is absorbed primarily at the beginning of the intestine and before gastric juice neutralization, while 60% of it is excreted through feces. Calcium absorption occurs in two forms, passive and active, through the intestines, and renal reabsorption takes place through the kidneys. Various factors such as intestinal environment, dietary components (including lactose, proteins, and amino acids), bile salts, parathyroid hormone, vitamin D, acidic pH, health status, age, and growth hormone influence intestinal calcium absorption positively. Conversely, fatty acids, phytic acid, aging, alkaline pH, iron, magnesium, calcitonin hormones, and glucocorticoids reduce calcium absorption. Parathyroid hormone, calcitonin hormone, vitamin D, and dietary regimen significantly contribute to the active reabsorption of calcium through renal tubules. Despite the considerable variations in the calcium content of dietary sources, a highly precise regulatory system controls vitamin D production, preventing fluctuations in plasma calcium ion concentrations. This regulation helps prevent hypocalcemia and hypercalcemia, which can lead to numerous irregularities in the body.

Keywords: Calcium, Absorption, Reabsorption, Intestine, Kidneys, Hormones, and Diet

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Introduction

The human body is composed of various elements and compounds, with calcium being one of the vital and essential minerals. On average, the body contains approximately one kilogram of calcium. Most of the calcium (about 99%) is present in the form of crystals, combined with phosphates, in the structure of bones (calcium phosphate 85%, calcium carbonate 10%, calcium fluoride 0.3%, and calcium chloride 0.2%).[11] The remaining one percent is found in the body's blood, interstitial fluids, and tissues. Calcium constitutes about 1.5 to 2% of body weight and makes up approximately 39% of all body salts.[14]

Bones are active tissues constantly engaged in exchanges with the external environment, serving as a significant reservoir for calcium storage in the body. In a normal and balanced state, the rate of calcium absorption into the bones is equal to the amount of calcium released during bone turnover. Approximately two percent of the calcium in bones exists as a readily exchangeable and mixable reserve with calcium in the extracellular fluids.[6]

Calcium in the plasma exists in three forms: ionized, bound to proteins (albumin), and as complexes with organic acids. The ionized form of calcium is the only active form in body fluids. In addition to its role in bone and teeth structure, calcium plays a crucial and vital role in numerous biochemical and physiological activities, including nerve-muscle excitability, blood clotting, bodily secretions, permeability of cell membranes, enzymatic reactions, hormone secretion, as a secondary messenger in hormonal signaling, milk production, nerve signal transmission, weight reduction, blood pressure regulation, cancer prevention, and cholesterol absorption reduction.

Calcium is abundantly present in nature and in food sources. The daily requirement of calcium for the human body is obtained through the diet and absorbed by the intestines. Various hormonal and non-hormonal factors influence intestinal and renal calcium absorption.[4]

Disruptions in the process of calcium absorption can lead to hypercalcemia or hypocalcemia, resulting in various

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metabolic bone disorders. Therefore, to prevent irregularities caused by changes in calcium absorption, maintaining normal blood and body fluid calcium concentrations and identifying factors involved in calcium absorption are crucial. The subject of my research is "Factors Affecting Intestinal Absorption and Renal Reabsorption of Calcium in the Body," and I conducted extensive research on this topic in a library setting, utilizing reputable scientific sources, to provide valuable and effective insights for enthusiasts in the fields of chemistry and biological sciences.[4]

Absorption of Calcium

Calcium absorption occurs through the intestines and its reabsorption takes place by the renal tubules.

- Calcium entering the body through diet is mostly in the form of phosphates, carbonates, and tartrates. Calcium absorption is less efficient than the incomplete absorption of sodium and potassium. Approximately 40% of the ingested calcium is absorbed through the intestines and excreted.[4] Calcium absorption primarily occurs in the beginning of the small intestine (duodenum) and before gastric juice becomes completely neutral (pH = 2-7). Most insoluble organic and inorganic calcium salts, aided by gastric secretions, dissolve within the stomach. Therefore, calcium chloride and acidic phosphate are absorbed in the duodenum before the gastric contents are fully neutralized.[5]
- The kidneys filter approximately 250 mmol of calcium ions daily, with about 95% of it being reabsorbed through the renal tubules.[4]

The Mechanism of Calcium Absorption

There are two mechanisms for calcium absorption:

- Simple diffusion
- Active transport which is carried out with the expenditure of energy using calcium pumps.

Both mechanisms rely on 1,25-$(OH)_2D_3$, as this vitamin regulates the synthesis and spread of calcium-binding proteins and a calcium ion-dependent ATPase.[4]

The Effective Factors for Absorption of Calcium

The three important components of the body, namely the skeletal system, the small intestine, and the kidneys, play a fundamental role in regulating the absorption and concentration of calcium in the body.[2] The absorption of calcium by the intestines and the reabsorption of calcium by the kidneys are influenced by various factors. These factors are divided into two categories:

- Factors that increase the absorption of calcium in the body through the intestines or kidneys.
- Factors that lead to a reduction in the absorption and increased excretion of calcium from the body.

Effective factors for Absorption of Calcium Through the Intestines

- Calcium concentration in intestinal content: The higher the calcium intake, the lower the absorption of calcium.[12]
- Presence of lactose in food: Lactose produces lactic acid and increases the absorption of calcium.
- Presence of protein in the diet: In a protein-rich diet, more than 15%, and in others, 5% or less of dietary calcium is absorbed.
- Amino acids: Arginine and lysine amino acids dissolve calcium salts more effectively, increasing calcium absorption in the intestines.
- Bile salts: Bile salts that accelerate the digestion and absorption of fats also increase calcium absorption.
- Bacteria: The presence of acidophilic bacteria (Lactobacillus).
- Calcium-to-phosphorus ratio: The ratio of calcium to phosphorus concentration in food is crucial for the absorption of these two elements. A higher ratio results in more calcium coming in as non-soluble phosphate. The most suitable calcium-to-phosphorus ratio is 1 (Ca/P = 1) or approximately 0.5 to 2.[5]
- Parathyroid hormone (PTH): Parathyroid hormone, synthesized and secreted by the parathyroid gland, is a polypeptide containing 84 amino acids. Its secretion is inversely related to the ion concentration of calcium. This hormone indirectly affects calcium absorption by affecting the intestines.[4] An increase in PTH in the bloodstream leads to increased production of vitamin D3 and, in turn, increases calcium absorption, its retention by the kidneys, and its removal from bones.[14]
- Vitamin D3: Vitamin D is derived from cholesterol and its active form is calcitriol 1,25-$(OH)_2D_3$, which acts as a hormone. Its primary role is to increase the absorption of calcium and phosphates in the mucous membrane of the intestines. Despite variations in the calcium content of foods, a highly precise regulatory system, influenced by changes in plasma calcium ion concentration, ensures the adequate levels of calcium and phosphates necessary for bone formation and calcium crystal deposition within collagen fibers in bones.[6] It also plays a very important role in maintaining plasma calcium and phosphorus levels within the normal range. About 80% of the required vitamin D is obtained from exposure to sunlight on the skin. However, this amount may decrease due to factors such as skin color, climate conditions, habits, and sun avoidance. Vitamin D deficiency in children and adults can lead to softening of the bones,[9] so adequate amounts of this vitamin are essential for optimal calcium absorption. Vitamin D has many other effects on various organs and systems in the body.[1]
- Intestinal pH: Calcium absorption is facilitated in an acidic environment because calcium salts, especially phosphates and carbonates, are completely soluble in an acidic medium.
- Other substances: High-protein foods, carbohydrates, and organic acids such as citric acid facilitate calcium absorption by increasing the solubility of calcium ions.
- Health status and age: In childhood and adolescence, approximately 60% of dietary calcium is absorbed,[12]

while in healthy adults, about 40% of daily dietary calcium is absorbed. In individuals over sixty years old, the amount of calcium absorption is higher.[4]

- Growth hormone (GH): This hormone, produced and secreted by the anterior part of the pituitary gland, in addition to other biochemical activities, increases the intestinal absorption of mineral substances, especially calcium. As a result, it contributes to the growth and development of long bones and cartilage in children and the transverse growth of these structures in adults.[4]
- Wheat products: Consuming wheat products with calcium-containing foods increases calcium absorption.

Factors balance or reduce Calcium absorption through the intestines

- Fatty acids: The presence of excessive fatty acids leads to the production of poorly soluble calcium salts (soap) and reduces intestinal calcium absorption.
- Organic acids: The presence of phthalic acid (Inositol hexaphosphate) in cereal bran and oxalic acid in certain vegetables leads to insoluble calcium salts forming and hindering calcium absorption.[5]
- Alkaline environment: In an alkaline environment, calcium absorption decreases due to the formation of poorly soluble calcium phosphate salts.
- Other substances: Excessive iron, magnesium, and phosphate interfere with calcium absorption.
- Age: With increasing age, especially beyond sixty years, intestinal calcium absorption decreases.[4]
- Calcitonin hormone: This hormone is synthesized and secreted by the C cells of the thyroid gland. Its secretion depends on blood calcium concentration. Calcitonin lowers serum calcium levels and opposes the action of parathyroid hormone (PTH). It inhibits the synthesis of 1,25-$(OH)_2D_3$ and thus reduces calcium absorption through intestinal.[8]
- Glucocorticoids: These hormones, synthesized and secreted by the adrenal cortex just above the kidneys, reduce intestinal calcium absorption.[4]
- Caffeine: Caffeine reduces calcium absorption and increases its excretion.
- Alcohol: Alcohol reduces intestinal calcium absorption and inhibits the conversion of vitamin D to its active form.
- Phosphorus: The impact of phosphorus on calcium excretion is negligible, but the consumption of carbonated soft drinks can lead to bone softness and fragility.
- It's important to note how and to what extent various dietary components affect each other's absorption should not lead to the exclusion of certain foods, as a balanced diet can provide the body with the necessary nutrients.[12]

Reabsorption factors of calcium through kidneys

As previously mentioned, all kidneys filter 250 millimoles of calcium ions daily; however, 95% of it is reabsorbed by renal tubules. Most of the calcium is reabsorbed in the proximal convoluted tubules of the kidneys without hormonal control; however, precise control of reabsorption in the distal convoluted tubules of the kidneys is regulated by PTH. This hormone, through cAMP, increases calcium absorption in the distal convoluted tubules of the kidneys.[4]

Factors that play a role in the regulation of calcium reabsorption and excretion by the kidneys include:

- Parathyroid Hormone (PTH): Under the influence of this hormone, calcium reabsorption by the kidneys reaches over 98%.[6]
- Calcium-rich foods: Consumption of calcium-rich foods can lead to hypercalcemia, causing increased excretion of calcium through urine. If urinary calcium is low and serum calcium is above normal, familial hypocalcemia hypercalcemia may be suspected.[3]
- Calcitonin Hormone: Calcitonin is produced by the C cells of the thyroid gland and is a 32-amino acid polypeptide. Its concentration in the serum of healthy individuals is very low. The greatest effect of calcitonin is observed during fetal development and in children. Calcitonin causes a reduction in calcium, phosphate, sodium, potassium, and magnesium reabsorption in the kidneys, leading to increased calcium excretion through the kidneys.[3]
- Vitamin D_3 reduces renal calcium excretion while increasing intestinal and renal absorption of calcium.[8] In conjunction with PTH, it also increases calcium breakdown from bone tissue.[3]
- Sodium: Excessive salt consumption leads to increased calcium excretion through the kidneys.
- Proteins: As mentioned earlier, proteins enhance calcium absorption in the intestines; however, since blood calcium levels remain unchanged, proteins increase renal excretion of calcium.[12]
- Other Factors: Diet, seasons, medication use, kidney disorders, bone and dental diseases.[3]

The normal Concentration of Calcium in the body

Calcium in the plasma exists in three forms: ionized, bound to protein (albumin), and as complexes with organic acids. The ionized form is the only active form of calcium in the body. Its combined form with protein is crucial in maintaining calcium in solution and preventing its deposition in tissues.[4]

The normal calcium levels in the blood are 9–10.5 mg/dl in adults and 7-10.4 mg/dl in infants. An increase in serum calcium above the normal range is referred to as hypercalcemia.[7]

Increased calcium uptake from bones, increased absorption of calcium from the intestines, and increased reabsorption from the kidneys can cause hypercalcemia, while the opposite, hypocalcemia, can result from these processes.[2]

The initial symptoms of hypercalcemia may include nocturia (increased nighttime urination), polyuria (excessive

urination), and thirst. In severe hypercalcemia, loss of appetite, nausea, and vomiting can occur. Kidney stone formation and long-term bone pain and fragility may also be observed.[3] High blood calcium levels can lead to kidney dysfunction, calcium deposition in blood vessels and tissues, calcium excretion in urine, and impaired iron absorption.[12]

Suppose it is determined that the body's calcium levels are above normal. In that case, it can lead to conditions such as hyperparathyroidism, excessive secretion of PTH hormone by cancerous tumors, increased vitamin D, chronic kidney disease, and disorders of the parathyroid glands. Medications that induce hypercalcemia, such as thiazides and calcium-containing antacids, can also contribute to high calcium levels.[3]

Women in menopause, individuals with a sensitivity to cow's milk, and vegetarians are at risk of calcium deficiency. A deficiency in dietary calcium intake, lack of exposure to sunlight, excessive daily fiber intake exceeding 30 grams, high sodium intake, consumption of foods rich in oxalic acid, coffee consumption, prolonged periods of rest, pregnancy, immobility, reduced gastric acid secretion, and the use of diuretic medications can all lead to hypocalcemia. Symptoms of calcium deficiency in the body include bone weakness and softness, severe muscle contractions and cramps,[15] numbness in the fingers, significant loss of appetite, abnormal heart rhythms that can be fatal if not addressed, muscle cramps, and seizures. Long-term calcium deficiency can lead to bone fractures (Mousavi, 2017, p. 68), and in children, it can cause growth delay and mental retardation.[2]

Calcium-enriched foods and it's daily needs

The required amount of calcium varies by age and different conditions. It is recommended for infants and young children to consume 800 to 210 mg, while older children and adolescents should aim for 1300 mg. For adults, the recommended intake ranges from 1200 to 1000 mg.[15] According to the World Food Organization's recommendations, each individual's average daily calcium requirement is one gram.[1] During pregnancy and lactation, the daily need increases to 1.3 and 2 grams, respectively.[4] During physical exercise and for athletes and military personnel, the need for calcium is higher than normal. Intense physical activity can lead to calcium loss through sweat and an increased skeletal need for calcium. The effects of high-impact sports on bones are more pronounced during pre-adolescence.[14]

Reduction in calcium intake is a significant risk factor for certain diseases such as cancer, high blood pressure, insulin resistance, and obesity. Individuals with low dietary calcium intake have a higher prevalence of obesity and overweight.[13]

Calcium in foods is mainly found in mineral compounds and to a lesser extent in organic forms.[3] This element is abundant in food items such as milk, cheese, eggs, legumes, parsley, cream,[4] okra, broccoli, fish, nuts, and seeds like almonds and sesame, white beans, and dark leafy greens.[13]

Significance of Calcium

Calcium in the body serves the following functions:

- Involvement in the construction of bones and teeth.
- An important factor in blood clotting, and without its presence, blood clotting does not occur.
- Decreased permeability of capillary vessel walls and spaces.
- Acts as a cofactor for the activation of certain enzymes, such as lipase, succinate dehydrogenase, and ATPase.
- Reduced neuromuscular excitability.
- Calcium is essential for the normal transmission of nerve impulses and muscle contractions.
- Calcium prevents muscle tremors.[3]
- Muscle contraction and cardiac excitability.
- Serves as a secondary messenger in the activity of some hormones.[4]
- Nursing and pregnant women require higher amounts of calcium. Insufficient calcium in their daily diet can lead to decreased calcium in their bones and chronic pain. Calcium and vitamin D tablets alleviate this problem.[10]
- In body secretions and mucous membranes.
- Secretion and proper hormone activity.[6]
- High calcium intake is effective in reducing obesity and reducing the risks and consequences of obesity and weight loss in overweight individuals.[1]
- When taken in sufficient quantities together with other minerals, especially potassium, magnesium, etc., calcium helps lower blood pressure and regulate heart activity.[15]
- Calcium plays an effective role in preventing colorectal cancer and continues to be effective in reducing fat absorption from the intestines, excreting it, and lowering blood cholesterol levels in preventing cardiovascular diseases.[12]

Conclusion

Calcium is a vital element that plays a valuable role in the construction of bones and teeth, blood clotting, activating enzymes, nerve signal transmission, muscle contraction, heart excitability, acting as a secondary messenger in the activity of certain hormones, milk production, fetal growth, hormone secretion, bodily secretions, and cell membranes. It also contributes to reducing obesity and the associated risks and consequences of obesity in overweight individuals, among other functions, and should be introduced into the body through daily dietary intake. The absorption of dietary calcium through the intestines is incomplete, with only about 40% being absorbed, and the remainder is excreted through feces. Various factors such as the calcium concentration in the intestines, the presence of lactose, proteins, and amino acids in food, bile salts, acidophilic bacteria, parathyroid hormone, vitamin D, acidic pH, overall health status, age, and growth hormone can increase intestinal calcium absorption. Conversely, fatty acids, phthalic acid, oxalic acid, alkaline environment, iron, magnesium, calcitonin hormones, and

glucocorticoids decrease calcium absorption through the intestines. Hormonal and non-hormonal factors influence calcium reabsorption through renal tubules. Suppose there is a disruption in intestinal absorption or renal reabsorption of calcium in the body. In that case, it can lead to hypocalcemia and hypercalcemia, which have adverse consequences and manifest as illnesses. Therefore, in addition to ensuring dietary sources of calcium in daily meals, it is important to control and monitor factors that affect calcium absorption to prevent the adverse consequences of its deficiency or excess in the body.

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