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## Review Article

# Multiherb Containing Calcium Formulation

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## ABSTRACT

Calcium is a necessary vitamin for human health. It helps the body create strong bones and teeth. Calcium is also required for the correct functioning of your heart and other muscles. Calcium shortage, also known as hypocalcemia, is a disorder in which a person's blood calcium levels are abnormally low. Women, in particular, must begin increasing their calcium consumption earlier in life than males, beginning around middle age. As a woman approaches menopause, it is especially vital to meet her calcium requirements. Calcium homeostasis is important for supporting human life functions like skeleton maintenance, hormone secretion regulation, nerve impulse transmission, and vascular activity. Herbs with a high calcium content may aid in the maintenance of calcium levels in the body. Although there are a variety of supplements available to address calcium shortage, herbal formulations are recommended since they have less side effects and are less expensive. This research focuses on the use of herbal plants to treat hypocalcemia. The goal of this study was to produce and test herbal sweets that contained these herbs and used natural excipients. Drumstick (*Moringa oleifera*), shingada (*Trapa natans*), hadjod (*Cissus quadrangularis*), and finger millet (*Eleusine coracana*) are among the ingredients in the formulation that have been shown to help with hypocalcemia.

## INTRODUCTION

The fifth most prevalent element in the human body is calcium. After the age of 35, both men and women lose calcium from their bones. Menopause, on the other hand, accelerates the rate of loss in women. It also aids neuron function, blood coagulation, and muscular health.

Importance of Calcium Calcium is a crucial mineral for healthy bones. Nearly all of the calcium in the body is stored in the bones and teeth. Because of the mineral, they are tough and durable. The remaining 1% is required for a range of functions that maintain the body functioning properly. Calcium aids in the contraction (narrowing) and expansion of blood vessels,

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muscle contraction, nerve transmission, and gland hormone secretion. Because calcium insufficiency causes the entire matrix of the bone to weaken in women, maintaining a sufficient calcium intake in our diet can help women avoid osteoporosis after menopause [1,3]. Every day, calcium travels in and out of bones, causing them to be rebuilt. Because the body develops new bone faster than it breaks down existing bone in children and teenagers, overall bone mass increases. This continues until around the age of 30, when new bone production and old bone disintegration begin to occur at a similar rate. Calcium intake should be around 1000 mg per day; however, this demand increases during childhood growth, nursing, and pregnancy. Calcium is necessary for good health throughout the body. It is required by your body on a daily basis, not just to keep your bones and teeth strong throughout your life, but also to promote optimal muscle and nerve function [2]. With ageing, the dynamic of bone tissue metabolism changes dramatically. When a person is young, their bone mineral density (BMD) increases continuously until the third decade of life, when the osteoblastic activities are blocked. Although the best time for bone structural modelling is during puberty, the process continues, albeit to a lesser amount, as the body matures [3]. Women must begin increasing their calcium intake earlier than men once they reach middle age. It's crucial for women approaching menopause to increase their calcium intake. Calcium deficiency is a condition in which a person's blood calcium levels are abnormally low. Low calcium levels can cause a variety of health problems because calcium is a vital mineral that helps the body build healthy bones and teeth. Calcium shortage might also raise your chances of developing osteoporosis and osteopenia. Calcium shortage can be caused by a variety of circumstances, the most common of which is not getting enough calcium for lengthy periods of time. Age and genes are two more risk

factors. Calcium deficiency can also be caused by some drugs, an imbalanced diet or dietary intolerance to calcium-rich foods, and hormonal imbalance in women. It's important to ensure proper calcium intake at all ages. Calcium intake recommendations for children and teenagers are the same for both sexes. The daily allotment are as follows, according to the National Institutes of Health Trusted Source [4,5,6] The quantity of calcium required for good bones and teeth varies with age, according to the US government's dietary guidelines Trusted Source. The National Institutes of Health recommends these daily consumption recommendations for adults (4,6) Calcium Homeostasis Calcium consumption is around 1,000 mg per day on average, with 400 mg absorbed in the small intestine. Intestinal secretions discharge around 200 mg. The remaining 800 mg is eliminated in the faeces, leaving a net absorption of 200 mg (about 20%). The ECF and the bone exchange about 500 mg of calcium each day. The renal tubules resorb 9,800 mg (98%) of the 10,000 mg of  $\text{Ca}^{+2}$  filtered via the kidneys, and roughly 200 mg is expelled, which equals the net quantity absorbed in the small intestine [7]. Ca regulates neuron excitability, which is necessary for maintaining various important physiological functions [8]. i) Ca regulates nerve excitability. The peripheral neuromuscular system is primarily affected. Perfusing a muscle with Ca-free fluid can cause fibrillary twitching. The automatic ganglia become irritated as well. ii) It is required for the skeletal muscles to maintain their integrity. Increases in ionised Ca led to increased contractility, and vice versa. iii) It is critical for the heart's tone and contractility to be maintained. Ca counteracts the depressive effects of K. iv) It assists rennin in the stomach's milk coagulation. v) It is used to reduce exudation, which causes wheals, in allergic disorders. vi) Ca is involved in the development of some tissues and bones. Normally 25- 35% is



excreted in the urine and the rest in the stools.

**Hypocalcemia** Hypocalcemia is a common metabolic anomaly that can range in severity from asymptomatic to a life-threatening crisis in severe cases. Three key calcium-regulating hormones-parathyroid hormone (PTH), vitamin D, and calcitonin-control serum calcium levels within a tight range (2.1-2.6 mmol/L) via their particular actions on the intestine, kidneys, and skeleton. The remaining free ionised calcium is physiologically active, with approximately half of total serum calcium bound to protein. Before verifying the diagnosis of hypercalcemia or hypocalcemia, serum calcium values must be corrected for albumin levels. Patients with hypocalcemia may experience a variety of symptoms and indicators, as low serum calcium levels can affect practically every organ or system [9]. New onset hypocalcemia can be a life-threatening scenario that necessitates rapid medical attention, although chronic low serum calcium levels might be asymptomatic or mildly symptomatic. Identification, clinical assessment, and management of hypocalcemia are critical issues that must be addressed concurrently and as quickly as feasible in all cases. The goal of this paper is to provide a useful approach for clinical practise by updating the data on the diagnostic assessment and clinical management of hypocalcemia [10]. What are the symptoms of hypocalcemia? Calcium deficiency becomes more likely as you become older. Here are some of the other factors that put you at risk [11].

- For a long time, especially during childhood, there was insufficient calcium intake.
- Some drugs can reduce calcium absorption.
- Intolerance to calcium-rich foods in the diet
- Women's hormonal changes
- A number of genetic factors

Calcium deficiency is a condition in which a person's blood calcium levels are abnormally low. Low calcium levels can cause a variety of health problems because calcium is a vital mineral that helps the body build healthy

bones and teeth. Calcium shortage might also raise your chances of developing osteoporosis and osteopenia [2]. Calcium shortage can be caused by a variety of circumstances, the most common of which is not getting enough calcium for lengthy periods of time. Age and genes are two more risk factors. Calcium deficiency can also be caused by some drugs, an imbalanced diet or dietary intolerance to calcium-rich foods, and hormonal imbalance in women [1]. What is clinically relevant hypocalcaemia? The serum calcium concentration must be interpreted in relation to serum albumin. Serum calcium exists in an ionised form (50%) or is bound to albumin or other ions. Only ionised calcium is biologically important. Various factors alter the ratio of ionised calcium to bound calcium, but the most important factor is the albumin concentration. Many medical conditions cause a decrease in serum albumin. Serum calcium concentrations are therefore "corrected" to a reference albumin concentration of 40 g/l, and for every 1 g/l of albumin above or below this value, the calcium is adjusted by decreasing or increasing by 0.02 mmol/l [12].

## CAUSES OF HYPOCALCAEMIA

Hypocalcaemia with low vitamin D concentrations Hypocalcaemia can develop in persons who don't get enough ultraviolet radiation, especially if they eat a vitamin D-deficient diet. The need for vitamin D rises during and after pregnancy. In breastfed children, low maternal vitamin D levels are linked to hypocalcaemia. Some patients receiving antiepileptic medicines, which induce enzymes that promote vitamin D metabolism, develop hypocalcemia due to vitamin D shortage. The frequency of vitamin D deficiency was found to be 75% in a study of institutionalised children with poorly managed epilepsy. Osteomalacia was likely caused by inadequate nutrition and limited sun exposure [10]. Hypocalcaemia with reduced parathyroid hormone function Patients with



decreased parathyroid gland function develop hypocalcemia. It's most common after thyroid or parathyroid surgery, although it can also be idiopathic, occurring predominantly in young adults and less frequently as part of a hereditary disease like autoimmune polyglandular syndrome. Reduced parathyroid hormone levels resulted in increased renal calcium loss and decreased intestinal calcium absorption as a result of decreased 1,25-dihydroxyvitamin D synthesis [13]. Hypoparathyroidism is a rare condition, with prevalence rates ranging from 5.3 per 100,000 to 37 per 100,000 people each year, depending on the community investigated. Hyperphosphatemia and abnormally low or low-normal serum PTH levels are linked to hypocalcemia [10]. Hypocalcemia can enhance both central and peripheral neuronal excitability, resulting in two forms of convulsive seizures. First, the patient may have a seizure disorder identical to that of someone who does not have hypocalcemia. Second, systemic tetany can develop into protracted tonic spasms, often known as cerebral tetany [14]. Forms of serum calcium  $\text{Corrected total serum Ca}^{+2} (\text{mg/dl}) = \text{measured serum Ca}^{+2} (\text{mg/dl}) + 0.8 (4.0 - \text{serum albumin g/dl})$  [7]. Hormonal regulation of calcium homeostasis Three mechanisms are required for  $\text{Ca}^{+2}$  homeostasis: intestine absorption, bone turnover, and renal reabsorption. The parathyroid hormone (PTH), calcitriol (the most active form of vitamin D), and blood ionised calcium are the hormonal regulators of these processes. The PTH receptor (PTHr), vitamin D receptor (VDR), and calciumsensing receptor (CaSR) are the receptors for these hormonal regulators, respectively [7]. Vitamin D, metabolism, and maintenance of calcium homeostasis Vitamin D is obtained via fortified dairy products and fish oils in the diet, or it is produced in the skin by ultraviolet irradiation from 7-dehydrocholesterol. Vitamin D binding protein transports vitamin D throughout the bloodstream. The active form of vitamin D, 1,25

(OH) $2\text{D}_3$ , requires a succession of hydroxylations, the first at the 25th carbon and the second at carbon 1. The synthesis of 25-hydroxyvitamin D [25(OH) $\text{D}_3$ ], the predominant circulating form of vitamin D and the most reliable measure of vitamin D status, occurs when vitamin D is 25-hydroxylated in the liver. CYP2R1 is now thought to be the primary enzyme in the conversion of vitamin D to 25 (OH) $\text{D}_3$  [15].

### Bone Calcium Regulation

Aside from intestinal and renal calcium absorption, bone resorption is an essential process for controlling calcium levels in the blood. Osteoblasts and osteoclasts are constantly remodelling bone. Osteoblasts help build bones, whereas osteoclasts tear down bone tissue and release calcium [16].

### FORMULATION OF HERBAL CANDY FOR TREATMENT OF HYPOCALCEMIA

Ayurvedic medicine commonly includes candies for the early treatment of hypocalcemia or calcium shortage. Candy is simple to administer. It requires minimum equipment, resulting in lower production costs. The formulation and evaluation of herbal hard candy created by moulding for the treatment of hypocalcemia are discussed in this research article.

### Importance of Herbal Candies

An herb is a plant or a component of a plant that is used for medicinal, aromatic, or savoury purposes. Nature provides a variety of foods for each season. Their use throughout that season proves to be quite advantageous to mankind, as they contain numerous medical benefits. Herbal pharmaceuticals play a significant part in Indian health systems; about 70% of current medicines in India are derived from natural ingredients. Herbal remedies have been increasingly popular in recent



years. The herbs used in herbal candy are chosen for their function in the treatment of altitude-related health issues with minimal side effects, as well as their availability and preference. Herbal products are far superior to allopathic medications. Herbal products have fewer negative side effects and provide more medicinal benefits [17].

### **Role of selected drugs in the treatment of altitude health problems**

The plants will be chosen for their function in the treatment of altitude-related health problems with minimal adverse effects, as well as their availability and preferences. The following plants are discussed:

- 1) Drumstick *Moringa oleifera* is an Indian plant that grows in tropical and subtropical climates around the world. Mother's best friend, often known as 'drumstick tree' or 'horseradish tree' [18]. Every portion of the tree is suitable for nutritional or economic applications due to its high nutritious properties. This study's scientific endeavour sheds light on the usage of moringa as a hypocalcemia treatment and the fortification of moringa oleifera in commercial products. Water-soluble vitamins (folic acid, ascorbic acid, and pyridoxine), fat-soluble vitamins (carotenoids, vitamin-D, and vitamin-E), minerals (iron, zinc, calcium, copper, magnesium, potassium), and phytochemicals (flavonoids, tannins, sterols, saponins, alkaloids, and anthraquinones) are abundant in *Moringa oleifera* leaves [19]. The dry leaves of *Moringa oleifera* contain 2185 mg/100 mg calcium. It has anti-cancer, anti-inflammatory, antidiabetic, and antibacterial properties. Seed of *M. oleifera*, a natural coagulant [20].
- 2) Shingada - Water chestnut buffalo nut, bat nut, devil pod, ling nut, lin kok, ling jow, ling kio nut, moustache nut, or singhara are some of its other names. The seeds have a calcium value of 102.85 mg/100 gm [21]. Glutamic acid, tryptophan, tyrosine, alanine, lysine, and leucine were frequent free amino acids detected in both kinds. Singhara contains antioxidants and has anticancer, antiviral, and antibacterial effects. This supports the spleen and stomach, as well as removing cancer, lethargy, sleeplessness, and a poor taste. Singhara can also be used to treat and relieve the symptoms of a weakened spleen. It also reduces the risk of heart disease and cures urinary infections [22].
- 3) Hadjod - Hadjod, also known as *Asthisamharaka*, is a delectable herb native to India's tropics. The hadjod contains iridoids, alkaloids, flavonoids, stilbene derivatives, sterols, triterpenes, fatty acids, methyl esters, and other phytochemicals. Hadjod powder contains 39.5 mg of calcium per 100 gm. Hadjod is well-known for promoting bone development and providing strength. It lowers the chances of fractures and muscle strain. In numerous animal models, Hadjod has been proven to have antiarthritic properties. Hadjod extract was discovered to have antiarthritic properties, lowering bone and cartilage degeneration, excessive paw inflammation, and the biochemical and haematological changes that go along with it. Hadjod is also utilized as an antioxidant, anti-inflammatory, asthma, epilepsy, blood sugar control, diabetes, and other medicinal purposes [23,24].
- 4) Finger millet-Finger millet is one of the calcium-dense foods, having three times the calcium content of milk. It is also the only grain with a consistent calcium concentration



across types (364 58 mg/100 g). As a result, finger millet has the ability to help calcium-deficient types. Finger millets contribute very high calcium retention and highly high bioavailable calcium, regardless of processing method, and may be beneficial for healthy growth and the treatment of calcium shortage issues [25]. Among the tiny millets, finger millet has the highest calcium level (300-350 mg/100 g) [26,27].

## LITERATURE VIEW

1. Gabriela C. in 2019 was explained about importance of calcium and helped to achieve calcium intake recommendations which involve major health benefits to individuals and populations
2. Munro P. in 2010 was reviewed on calcium balance and homeostasis and their relationship to dietary calcium intake.
3. Clinical study was done about diagnosis and management of hypocalcaemia like who gets hypocalcaemia and causes of hypocalcemia by Gittoes N.J.L. et al in 2008.
4. Level of serum calcium concentration and its causes were discussed by Goldstein D.A. in 2018.
5. Jane H. Kass-Wolff 2004 was demonstrated that young women's intake of calcium is significantly below the recommended dietary intake and reviewed on the role and functions of calcium, how it is transported
6. 7. Kumar D.S. et al in 2016 were described about the leaves of *Moringa oleifera* contains high level calcium and other medicinal applications. Elena G. B. et al in 2021 were investigated nutritional value of *Moringa oleifera* leaf powder extract and their neuroprotective effects via antioxidative and mitochondrial regulation.

8. Brahmshatriya M.H. et al in 2015 were performed clinical evaluation of *Cissus quadrangularis* is an indigenous medicinal plant which helps to increase healing process of fractured bone.

9. MD. Alfasane A. et al in were demonstrated that, *Trapa bispinosa* could be important sources of calcium, protein and minerals, which is suitable for incorporation in human diet.

10. Puranik S. et al in 2021 were reviewed on the importance of calcium and strategies to prevent calcium deficiency. Discussed in brief about the use finger millet as a model for calcium biofortification and prospecting bioavailability of calcium from biofortified finger millet to achieve adequate intakes.

11. Patil Madhuri et al in 2020 were studied with preparation of herbal candy as immune booster for cancer therapy. They were performed evaluation test of formulation; this might help us to get information about evaluation testing.

12. Calcium metabolism was described in detail by Mohammad Tinawi in 2020. Calcium homeostasis and calcium distribution in the body was given there.

## OBJECTIVES OF THE STUDY

To select plants containing calcium

To formulate herbal preparation for hypocalcemia

To provide natural supplement

## PLAN OF WORK

Selection of plant depending upon literature

Processing of plant material

Selection of appropriate formulation

Formulation of candy Analysis of formulation



## DISCUSSION

Herbal candy is prepared for the treatment of hypocalcemia especially for women because they have a lower bone density than men so they need a regular source of calcium to keep their bones sturdy. Four herbs were selected for making candy on the basis of their role and importance in the treatment of hypocalcemia. Various drugs are used in the treatment of hypocalcemia and the type of calcium in supplements and how efficiently it dissolves in the body impact the amount of calcium absorbed from them. The most common calcium compounds are calcium carbonate and calcium citrate. Calcium carbonate supplements dissolve more quickly in an acidic environment. Calcium citrate supplements can be used at any time because they do not require acid to dissolve. As a result, calcium citrate rather than calcium carbonate should be used by patients who have problems absorbing medications. This includes persons who take acid-reducing medicines (such as over the counter and prescription heartburn medications). In frequent doses, calcium supplements can cause bloating, gas, and constipation. Calcium in excessive amounts can cause kidney stones. Some studies suggest that supplementing calcium with a calcium-rich diet may raise the risk of heart attacks and strokes, whereas others disagree. If you have renal disease, heart problems, sarcoidosis, or bone cancers, you should avoid calcium supplements. High calcium levels in the blood can cause nausea, dry mouth, stomach pain, an irregular heartbeat, confusion, and even death. The four herbs selected for making candy are *Moringa oleifera*, *Trapa natans*, *Cissus quadrangularis*, and *Eleusine coracana*. The herb *Moringa oleifera* is the most successful in the treatment of hypocalcemia, or a lack of calcium efficiency. Shingada, hadjod, and finger millet are calcium sources and antioxidants that help fractures heal faster. During preparation, all

materials were in powdered form and weighed. Jaggery used to form the base of candies by melting. Molten jaggery helps to suspend the herbal powders and also imparts hardness to the candies after congealing. Additionally, it serves as a flavouring agent in the formulation. Candy mixture after heating should be properly poured into the mold so that it does not stick to the surface of mold which may not be good for shape of candy for avoiding this add clove oil for greasing and it also serves as flavouring agent as well active constituent. After molding it should be During preparation, all materials were in powder properly placed in cooling rack. After 10 to 12 hours of molding candies can be removed from the mold with the help of hands (covered with gloves), then they packed in butter paper and placed in refrigerator for evaluation. Various types of evaluation done to check the quality of it. Evaluation included following parameters colour, taste, flavour, etc. Various physicochemical parameters were studied to evaluate the quality of formulation, although there are no separate physicochemical parameters for candies, parameters used for solid dosage forms are also applicable for it. Various parameters are average weight found to be 1.2 gm. Disintegration time is also an important factor, twenty candies were subjected to disintegration and the average disintegration time was found to be 4 minutes, it should not more than 15 minutes. During handling of any product hardness should be enough to tolerate mechanical shocks. Hardness measured by using Monsanto hardness tester which was found to be 9 kg/cm<sup>2</sup>. Formulation was subjected to friability testing using Roche friability test apparatus, it passes the test as it lost only 0.34% during the procedure which lies within the limit. After evaluation candy was subjected to phytochemical analysis, it was analysed for presence of carbohydrates, proteins, calcium by using general identification tests. all compounds



are present in the formulation. Using the EDTA titration method, the calcium content of the formulation was determined to be 0.08101 gm/0.5 gm. Calcium detection was also reported to be 1.97 % in 1 gm using atomic absorption spectroscopy in the laboratory. Overall, this is a suitable formulation for hypocalcemia especially for woman, which has number of advantages such as easy to handle and store, effective.

## CONCLUSION

The use of various herb specific doses throughout a regular regimen may be beneficial in the treatment of early calcium deficient symptoms. As a result, herbal formulations may be suggested for usage as a positive immunomodulator. *Moringa oleifera* leaves, hadjod, finger millet, and shingada are calcium sources, according to the literature. The created formulation was sampled and tested for several characteristics such as organoleptic qualities, weight homogeneity, friability, and disintegration. It's a combination of herbs high in minerals, antioxidants, and anti-inflammatory qualities. It is an herbal supplement that aids in the treatment of a number of bone metabolic problems caused by calcium shortage.

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