



CALCIDEFTM

Dicalcium Malate 400mg, Vit D2 400 IU, Folic Acid 100mcg, Glycine 10mg Tablets

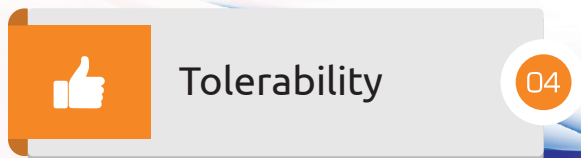
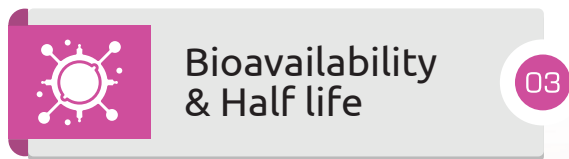
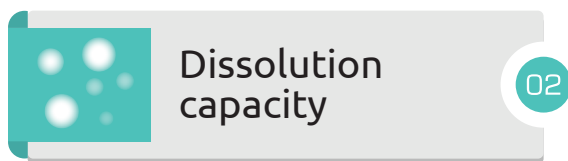
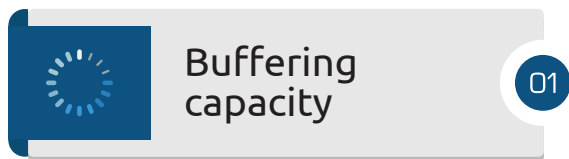
Calcium with a **DIFFERENCE**

**Are there any studies on
Calcidef vs other calcium salts?
Is there any study on absorption
of Calcidef vs other calcium salts?**



YES,

We have comparison against Ca carbonate showing superiority

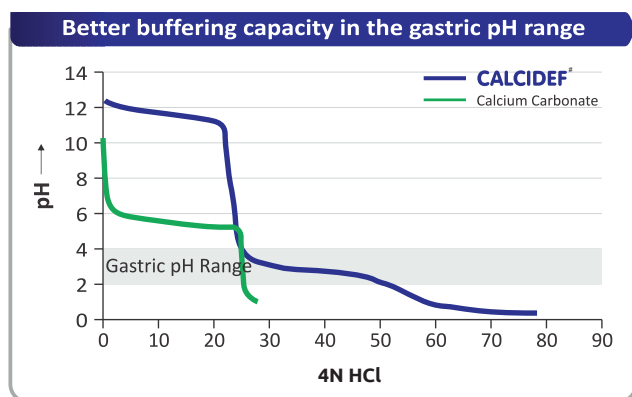


Dicalcium malate was compared with calcium carbonate in following studies.



Buffering capacity

Comparison of the two titration curves demonstrates that Dicalcium malate has buffering capacity in the gastric pH range. Calcidef would not have the gastric problems seen with calcium carbonate. Calcidef, due to its better buffering capacity in the gastric pH range, there is no acid rebound & gas formation.



In vitro dissolution study, comparing (Dicalcium malate 400 mg)



Dicalcium Malate 400 mg Tablets VS calcium carbonate 500 mg in different media.

Comparative Dissolution %, 45 min time point at end stage.		
Media	Calcidef (dicalciummalate 400 mg)	Calcium carbonate 500 mg
500 ml of 0.1 N HCl (gastric pH)	100.0	55.5
500 ml of 0.1N HCl, followed by 400 ml pH 4.5 Acetate Buffer	97.7	51.7
500 ml of pH 4.5 Acetate Buffer (pH under fed condition)	62.6	4.0
500 ml of Purified water	79.3	2.0
500 ml of pH 5.5 Citrate buffer (duodenal pH)	77.7	9.0
500 ml of 0.1N HCl , followed by 400 ml pH 5.5 citrate buffer	99.2	56.5



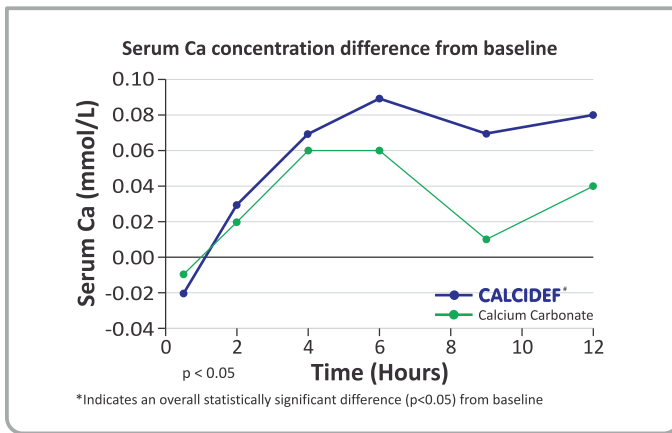
Bioavailability study



Equivalent doses of calcium carbonate and dicalcium malate were compared for bioavailability.

Calcidef showed statistically significant difference from baseline.

- Significant increase in calcium levels from baseline from 4 Hrs.
- Increase was not significant for Calcium carbonate

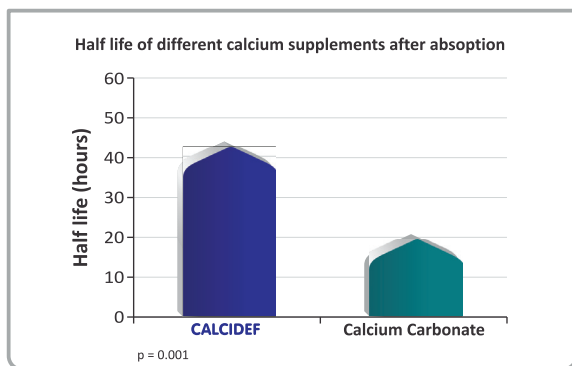


How the half-life of Calcidef is better than Calcium carbonate?

Both being Calcium supplements should have same half-life?



When equivalent doses of calcium carbonate and dicalcium malate were compared for bioavailability, it was observed that the serum level of Ca was also found to be elevated for a much longer time.



Supplement	Mean (Hour)	SD	P value
DimaCal*	42.48	16.25	-
Calcium Carbonate	20.00	8.04	0.001

Longer half-life which could be a reflection of the higher presence of the calcium in an absorbable form for a longer period.

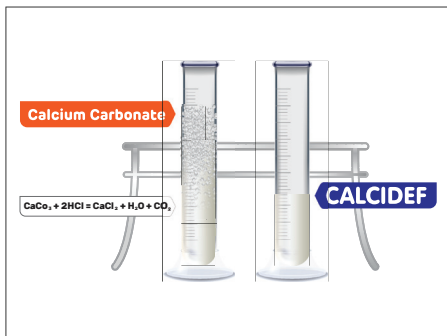
**Calcidef is bioequivalent form of Dimacal*

Tolerability



Equivalent doses of calcium carbonate and dicalcium malate when mixed with hydrochloric acid.

Calcium carbonate formed gas and frothing which was not seen with dicalcium malate



*Does not cause gastric problems
seen with Calcium carbonate*
 $\text{CaCO}_3 + 2\text{HCl} \rightarrow \text{CaCl}_2 + \text{CO}_2 + \text{H}_2\text{O}$

No CO_2 Production › No gastric problems

How Dicalcium malate is different than Calcium citrate & coral calcium?



Dicalcium malate is a salt of calcium providing 29% of elemental calcium (400mg) and is better absorbed than calcium carbonate.

Coral calcium is a salt of calcium derived from fossilized coral reefs (primarily from limestone and coastal deposits). Coral calcium is merely calcium carbonate. Calcium carbonate provides 40 percent elemental calcium; the other 60 percent is the carbonate ingredient.

Calcium citrate another salt of calcium provides 21% of elemental calcium and better absorbed than calcium carbonate in patients with higher gastric pH.



Recommended Dietary Allowance (RDA) of Calcium is 800-1000 mg/Day, Calcidef provides 400 mg. Then how does it meet RDA?



Calcium absorption is best when a person consumes no more than 500 mg at one time.*

- Each tablet of Calcidef, provides 400 mg of elemental calcium.
- It is assumed that rest of the calcium will come from diet or food.
- In chronic deficiency Dr can prescribe Twice daily. Since Calcium is mineral. So giving twice daily won't harm patient. (Its upto Dr discretion)

**National Institutes of Health. Office of Dietary Supplements. Calcium: Dietary supplement fact sheet. Reviewed November 21, 2013. <http://ods.od.nih.gov/factsheets/Calcium-HealthProfessional>. Accessed February 25, 2014 NIH*



Calcium carbonate has higher elemental calcium (40%) whereas dicalcium malate has only 29% elemental calcium. Then How dicalcium is better than calcium carbonate?



Not only is the calcium content but also its bioavailability is of essential importance.

Bioavailability, depends on the calcium solubility and extent to which calcium is available in absorbable form.

Effective absorption and bioavailability are extremely important if significant health benefits are to be derived from supplemental sources of calcium.

When calcium carbonate was compared with dicalcium malate, it was observed that dicalcium malate was significantly better absorbed than calcium carbonate.

The serum level of Ca were also found to be elevated for a much longer time. This indicates a longer half-life which could be a reflection of the higher presence of the calcium in an absorbable form for a longer period.

Calcium absorption is best when a person consumes no more than 500 mg at one time.

National Institutes of Health. Office of Dietary Supplements. Calcium: Dietary supplement fact sheet. Reviewed November 21, 2013. <http://ods.od.nih.gov/factsheets/Calcium-HealthProfessional>. Accessed February 25, 2014 NIH

Is Calcidef safe in renal patients?



There is paucity of data regarding usage of dicalcium malate in renal failure patients.

Patients with a history of kidney stones, who are taking calcium supplements, should have their urine monitored when they begin this therapy and check if the activity of their stone disease increases.

Kidney failure is known to disrupt a number of homeostatic mechanisms that control serum calcium and normal bone metabolism. Both negative and positive calcium balance have important implications in patients with chronic kidney disease, where negative balance may increase risk of osteoporosis and fracture and positive balance may increase risk of vascular calcification and cardiovascular events.

Given the available calcium balance data in this population, it appears clinically prudent to aim for recommended calcium intakes around 800-1000 mg/day to achieve neutral calcium balance and avoid adverse effects of either negative or positive calcium balance. For patients who fall below 800–1000 mg/day, modest increases in calcium from calcium-rich food sources, calcium supplements, calcium-based phosphate binders, or other calcium-containing medications might be considered.

Why only 400 IU of Vitamin D2 in Calcidef? Patients' needs more Vitamin D per week?



Dicalcium malate is licensed as food supplement.

Each tablet of calcidef, provides 400 IU of Vit. D2 which helps in calcium absorption.

It is assumed that rest of vit. D will be derived from Food or diet.

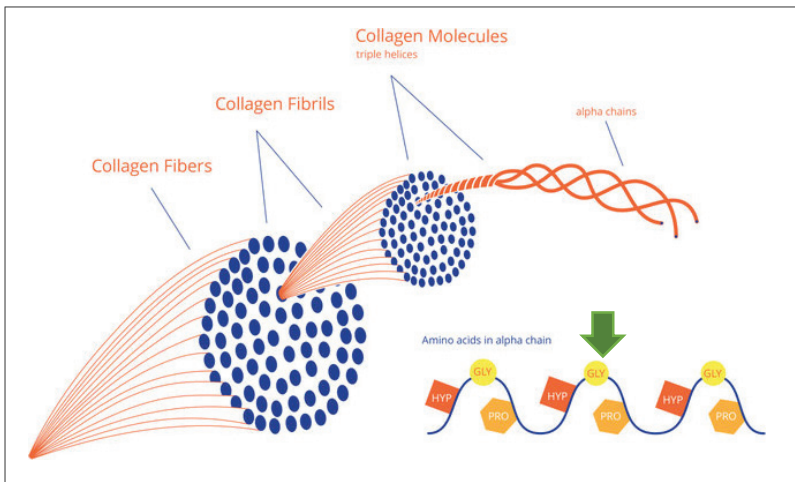
For patients with predominant Vit. D deficiency prescribe Vit. D well



What is the role of Glycine in Calcidef tablet?



Glycine is Simple proteinogenic (protein creating) amino acids and essential component of collagen fibers



Why only 10 mg Glycine in the combination?



Glycine is a simple amino acid. It is considered as "conditionally essential amino acid" because the body can make it from other chemicals.

Note: Average adult requires nearly 12-15 gms/day



If the Half-life of Dicalcium malate is 42.48hrs, can it be given once in two days?



Although half life of Calcium from our product is apparently more, after absorption from the gut it enter into blood.

In the blood calcium levels are very tightly regulated by multiple ways (absorption, distribution and excretion).

Thus calcium turnover is not solely dependent on absorption from gut, so it is prudent to take calcium daily.

Thus it suggested that calcidef can be taken daily.

Serum calcium concentration 8.5 -10.2 mg/dl.

<https://www.webmd.com/vitamins/ai/ingredientmono-1072/glycine>



Can Calcidef be given twice



Each tablet of Calcidef, will provides 400 mg of elemental calcium.

The molecular weight of calcium in dicalcium malate salt is 29%.

As calcidef has better bioavailability and half-life, supplement should be taken once daily.

Note: In chronic Ca deficiency it can be given BID, at the discretion of physician.



Is Calcidef associated with stone formation?



There is paucity of data on association of Dicalcium malate (DCM) and formation of urinary stones.

Calcium intake is one of the most misunderstood factors related to urinary stone formation. Hypercalciuria is the most common abnormality in calcium stone formers, several mechanisms can lead to hypercalciuria, as calcium homeostasis is primarily regulated through a complex interrelated interaction between the intestines, kidney, and bones.



Calcium intake and oxalate stone formation



There are evidences that dietary calcium intake is a protective factor against stone formation. It thought that dietary calcium restriction as it may lead to increased oxalate stone formation potentially through increased oxalate absorption. Oxalate absorption occurs throughout the intestinal tract.

When calcium and oxalate are consumed at the same meal, a calcium oxalate complex forms within the intestinal tract limiting the intestinal absorption of free oxalate. However, with dietary calcium restriction, free oxalate becomes increasingly available for intestinal absorption, leading to greater urinary excretion of oxalate.

Sorensen MD. Calcium intake and urinary stone disease. Transl Androl Urol. 2014;3(3):235-240. doi:10.3978/j.issn.2223-4683.2014.06.05

Abstract, flowing, wavy lines in shades of blue and white sweep across the bottom of the slide, creating a sense of movement and depth.

What is the effect of Calcidef on Iron absorption?



Studies on human subjects have shown that calcium (Ca) can inhibit iron (Fe) absorption, the precise mechanisms by which calcium impairs iron absorption are unclear.

However any inhibitory effect of the calcium is largely offset by the enhancers such as citric and ascorbic acids. Organic acids like malic acid are known to enhance iron absorption. Thus malate (malic acid) in Calcidef, may offset the inhibitory effects of calcium on iron absorption.

Secondly thorough review of studies on humans in which Ca intake for long periods shows no changes in iron status. Thus, the inhibitory effect may be of short duration and there also may be compensatory mechanisms.

Lönnnerdal B. Calcium and iron absorption--mechanisms and public health relevance. Int J Vitam Nutr Res. 2010 Oct;80(4-5):293-9. doi: 10.1024/0300-9831/a000036

Manya S Deehr, Gerard E Dallal, Kenneth T Smith, John D Taulbee and Bess Dawson-Hughes. Effects of different calcium sources on iron absorption in postmenopausal women. Am J Clin Nutr 1990;51:95-9

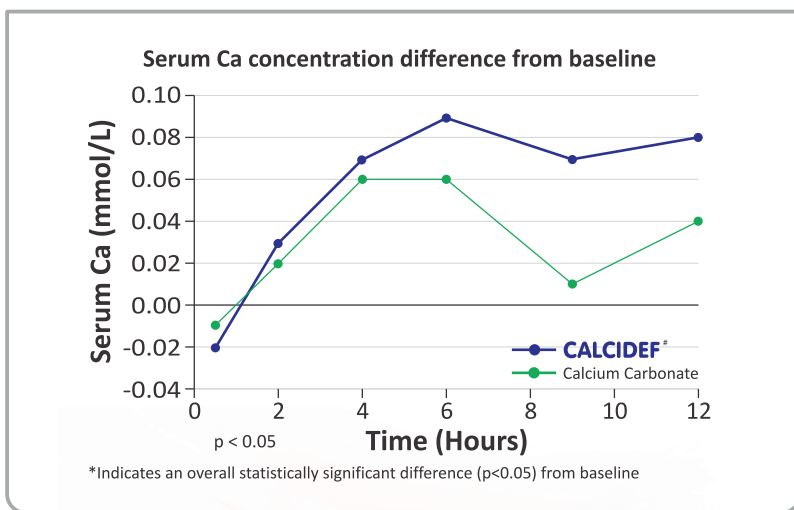
Lynch SR Interaction of iron with other nutrients. Nutr Rev. 1997;55:102- 110

Salovaara S, Sandberg AS, Andlid T. Organic acids influence iron uptake in the human epithelial cell line Caco-2. J Agric Food Chem. 2002 Oct 9;50(21):6233-8

What is exact bioavailability of Calcidef?



When the equivalent doses of calcium carbonate and dicalcium malate were compared for bioavailability. Calcidef showed statistically significant difference from baseline



Is there any impact of Calcidef on Calcium channel blockers (CCB)?



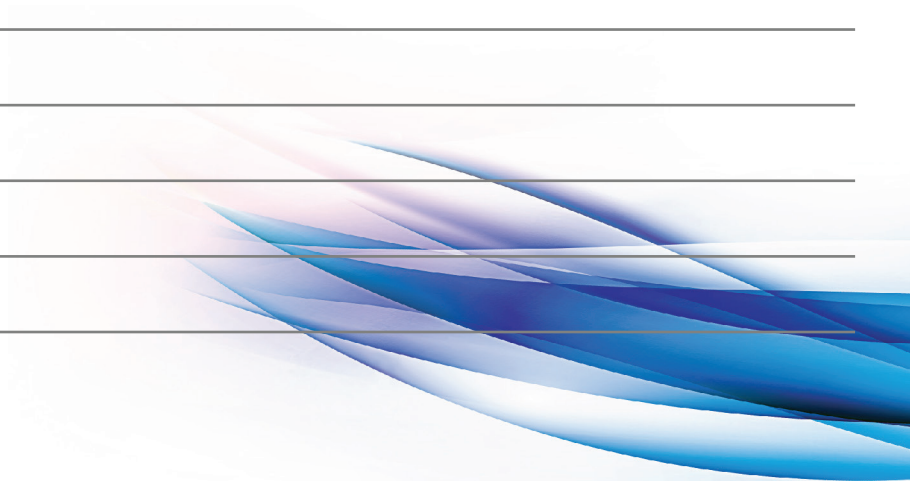
There's no evidence that oral calcium supplements interfere with calcium channel blockers. To be safe, check your blood pressure regularly if taking calcium channel blockers and calcium supplements at the same time.

In large amounts, calcium supplements may interact with thiazide and calcium channel blockers. In fact high doses of intravenous calcium are sometimes used to reverse an overdose of a calcium-channel blocker, the 600 mg of calcium in daily supplement isn't enough to interfere with the drug's ability to lower blood pressure.

Also calcium supplements don't appear to interact with other commonly prescribed blood pressure medications, such as: Beta blockers, Angiotensin-converting enzyme (ACE) inhibitors, Angiotensin II receptor blockers, Renin inhibitors.

Information available from <https://www.mayoclinic.org/diseases-conditions/high-blood-pressure/expert-answers/calcium-supplements/faq-20058266#:~:text=In%20fact%2C%20I%20calcium%20is,supplements%20at%20the%20same%20time>. accessed on 2 July 2020





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CALCIDEFTM

Dicalcium Malate 400mg, Vit D2 400 IU, Folic Acid 100mcg, Glycine 10mg Tablets

Calcium with a **DIFFERENCE**



CLASSIC
a SUN PHARMA division

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