Does Famotidine increase the amount of vitamin D that gets to cells? Note 1: Apparently, all of the following are known to increase vitamin D in cells: Resveratrol, Omega-3, Magnesium, Zinc, Quercetin, Curcumin, Berberine, Butyrate, Sulforaphane, and Metflormin. Note 2: All of the following genes affect the amount of vitamin D in the blood that gets to the cells. CYP27B1, CYP3A4, CYP24A1; Vitamin D Binding Protein, VDR. Note 3: Only two Vitamin D genes affect how much vitamin D gets measured in the blood: CYP27A1 and CYP2R1

🕅 perplexity

The Impact of Famotidine on Vitamin D Cellular Availability: A Comprehensive Analysis

In evaluating whether famotidine increases the amount of vitamin D that reaches cells, careful examination of current scientific evidence is required. This report analyzes the relationship between famotidine, a histamine H2 receptor antagonist commonly used to treat conditions like peptic ulcers and gastroesophageal reflux disease, and vitamin D metabolism, transportation, and cellular availability.

Famotidine's Pharmacological Properties and Mechanism of Action

Famotidine functions primarily as an H2 receptor antagonist, blocking the action of histamine on H2 receptors expressed on parietal cells in the stomach. This blockade inhibits gastric acid secretion by preventing histamine-induced activation of proton pumps^[1]. Unlike many medications that interact with cytochrome P450 enzymes, the search results do not specifically indicate that famotidine significantly interacts with CYP3A4 or other enzymes involved in vitamin D metabolism. Famotidine has incomplete oral bioavailability (40-50%), reaches peak concentration within 1-4 hours after administration, and has relatively low protein binding (15-22%)^[1].

Vitamin D Metabolism and Cellular Pathways

Understanding how famotidine might affect vitamin D requires knowledge of vitamin D metabolism pathways. Vitamin D undergoes several transformations in the body, with key enzymes including CYP27A1 and CYP2R1 (which affect blood levels), and CYP27B1, CYP3A4, and CYP24A1 (which influence cellular availability)^{[2] [3]}. After endogenous synthesis through sun exposure, vitamin D travels in plasma almost exclusively bound to vitamin D binding protein (DBP), which affects hepatic delivery and subsequent metabolism^[4].

The active metabolite 1,25-dihydroxyvitamin D (1,25(OH)2D) interacts with the vitamin D receptor (VDR) to regulate gene expression. This complex forms a heterodimer with the retinoid X receptor (RXR), which binds to vitamin D response elements (VDREs) in the promoter regions of target genes^[5]. The expression of enzymes such as CYP3A4 is regulated by vitamin D, creating potential for drug interactions since CYP3A4 metabolizes approximately half of all therapeutic drugs^{[5] [3]}.

Evidence Regarding Famotidine and Vitamin D Interaction

Current evidence does not directly demonstrate that famotidine increases vitamin D cellular availability. None of the search results explicitly state that famotidine enhances vitamin D transport to cells or increases its intracellular concentration. However, several indirect relationships warrant consideration.

Potential Indirect Effects on Vitamin D Status

One case report documents famotidine-induced hypomagnesemia leading to hypocalcemia^[6]. Since magnesium serves as a cofactor in several steps of vitamin D metabolism, including vitamin D binding to its transport protein, 25(OH)D synthesis, and 1,25(OH)2D synthesis^[7], famotidine-induced magnesium depletion could potentially impair vitamin D metabolism and cellular availability rather than enhance it.

Studies on famotidine's radioprotective effects indicate it acts as a powerful hydroxyl radical scavenger and prevents DNA damage^{[8] [9]}. These antioxidant properties might indirectly support cellular health, potentially maintaining cell membrane integrity and receptor function, but this does not necessarily translate to increased vitamin D cellular uptake.

Comparison with Known Vitamin D Enhancers

The query notes that several compounds are known to increase vitamin D cellular availability, including resveratrol, omega-3 fatty acids, magnesium, zinc, quercetin, curcumin, berberine, butyrate, sulforaphane, and metformin. Unlike these compounds, there is no evidence in the provided search results suggesting famotidine shares similar mechanisms for enhancing vitamin D transport or metabolism.

Role of Key Enzymes and Transport Proteins

The CYP24A1 enzyme is responsible for catabolism of vitamin D metabolites, while CYP27B1 converts 25-hydroxyvitamin D to the active form 1,25-dihydroxyvitamin D^[3]. Research has shown that inhibition of both CYP27B1 and CYP24 can increase the anti-proliferative effects of 25-hydroxyvitamin D3 in certain cell lines^[2], highlighting the importance of these enzymes in controlling vitamin D's cellular effects.

The vitamin D receptor (VDR) plays a crucial role in mediating vitamin D's cellular actions. VDR has physical interactions with β -catenin and regulates the expression of tight junction proteins such as claudin-2 and claudin-12^[10]. These interactions contribute to vitamin D's effects on tissue barriers and calcium homeostasis. However, no specific interaction between famotidine and VDR has been documented in the provided search results.

Clinical Implications of Histamine H2 Receptor Antagonists

While proton pump inhibitors (PPIs) have been associated with vitamin D deficiency—with one study showing 100% of long-term PPI users having vitamin D deficiency compared to 25% of controls^[7]—the evidence for H2 receptor antagonists like famotidine affecting vitamin D status is less clear. PPIs and H2 receptor antagonists differ in their mechanisms of action and potency in reducing gastric acid, which might result in different effects on nutrient absorption.

Famotidine has been studied for its radioprotective effects, with research showing it can reduce radiation-induced thrombocytopenia^[9] and protect against gamma-radiation-induced damage to mouse bone marrow^[8]. These effects appear to be mediated through its free radical scavenging abilities and prevention of DNA damage rather than through vitamin D-related mechanisms.

Conclusion

Based on the available evidence, there is insufficient support for the claim that famotidine increases the amount of vitamin D that reaches cells. In fact, the potential for famotidine to induce hypomagnesemia suggests it might indirectly impair vitamin D metabolism rather than enhance it.

The complex interplay between medications and vitamin D metabolism highlights the importance of considering drug-nutrient interactions in clinical practice. While many factors influence vitamin D status and cellular availability—including genetic factors, dietary intake, sun exposure, and medication use—the specific effects of famotidine on this system remain poorly characterized. Further research specifically examining the relationship between famotidine and vitamin D metabolism, transport, and cellular uptake would be valuable for clarifying any potential interactions.

For individuals concerned about optimizing vitamin D status while taking famotidine, monitoring vitamin D levels and ensuring adequate intake of nutrients that support vitamin D metabolism, particularly magnesium, may be prudent until more definitive evidence emerges.

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