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ACCURACY OF LABELED CALCIUM CONTENT IN MULTIVITAMIN BRANDS: A COMPREHENSIVE ANALYSIS WITH COMPLEXOMETRIC TITRATION

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Abstract
Calcium, a fundamental building block for strong bones and teeth, is often supplemented through multivitamins. This study evaluated the accuracy of labeled calcium content in five commercially available multivitamin brands, encompassing diverse formulations and price points. Complexometric titration revealed significant variations in measured calcium content across brands, ranging from X mg to Y mg (representing Z% to W% of labeled values). Notably, a substantial portion of the analyzed brands exhibited discrepancies between labeled and measured amounts. These findings raise concerns regarding consumer reliance on multivitamins to achieve the recommended daily intake (RDI) of calcium. The potential health consequences of inaccurate labeling and insufficient calcium intake are discussed. The study emphasizes the need for stricter regulations and improved quality control measures to ensure accurate labeling and safeguard consumer health.

INTRODUCTION

Importance of calcium:

Calcium is a crucial mineral, primarily found in bone, providing structure and supplying calcium to the skeletal system. Insufficient calcium intake can lead to bone health issues, such as rickets in children and fractures, osteopenia, and osteoporosis in older adults. [1]

Calcium is essential for muscle contraction, hormone and protein secretion, and neurotransmitter transmission. It maintains a steady pulse and particle movement. The amount of calcium needed depends on age, with children needing more calcium due to developing skeletal structures, while older individuals, especially women, are advised to take calcium supplements due to osteoporosis risk. Restorative conditions may also necessitate increased calcium intake. [2]

Calcium plays a role in: strengthening bones and teeth, regulating muscle functioning, such as contraction and relaxation, regulating heart functioning, blood clotting, transmission of nervous system messages, enzyme function.

Recommended intake of calcium:

These values, which change by age and sex, incorporate the taking after:

The Recommended Dietary Allowance (RDA) is the daily intake of nutrients that meet the nutritional needs of 97-98% of healthy people. This is used to create healthy diets. The Average Intake (AI) is the

intake that ensures adequate intake. The Estimated Average Requirement (EAR) is the daily intake that meets the nutritional needs of 50% of healthy people. The Tolerable Upper Intake Level (UL) is the highest daily intake that doesn't cause negative health effects. Recommended daily intake for men is 1,000 mg/day (25-65 years). For all women and men over 65, daily intake is recommended to be 1,500 mg/day, although further research is needed for this age group. [3]

Age	Male	Female	Pregnant	Lactating
0–6 months*	200 mg	200 mg		
7–12 months*	260 mg	260 mg		
1–3 years	700 mg	700 mg		
4–8 years	1,000 mg	1,000 mg		
9–13 years	1,300 mg	1,300 mg		
14–18 years	1,300 mg	1,300 mg	1,300 mg	1,300 mg
19–50 years	1,000 mg	1,000 mg	1,000 mg	1,000 mg
51–70 years	1,000 mg	1,200 mg		
>70+ years	1,200 mg	1,200 mg		
0–6 months*	200 mg	200		

*Adequate Intake (AI)

Objective:

The primary aim of the research is to evaluate the accuracy of labelled calcium content in various multivitamins, by doing we would know no reliable is our source of dietary works.

Complexometric titration:

EDTA (Ethylenediaminetetraacetic acid):

Complexometric titrations are used primarily to determine metal particles by utilize of complex-forming reactions. In spite of the fact that numerous complexing agents (cyanide, thiocyanate, fluoride, 1,2-diaminoethane, etc.) can be used for this reason, in practice the titrants are almost continuously compounds having the iminodiacetic acid functional groups. The foremost broadly connected are ethylenediaminetetraacetic acid, H4Y and the dihydrate of the sodium salt, Na2H2Y · 2H2O (better soluble in water). [4]

Ethylenediaminetetraacetic acid (EDTA) is a medication used in the management and treatment of heavy metal toxicity. It is in the chelating class of drugs. This activity outlines and reviews the indications, actions, and contraindications for EDTA as a valuable agent in managing lead toxicity.

EDTA or Ethylenediaminetetraacetic acid is commonly used as an indicator_for complexometric titration because it can act as a ligand which can bind to coordinate centers which are usually metals to form colored complexes. [5]

LITERATURE REVIEW:

Accuracy of nutritional labelling in dietary supplements:

The Dietary Supplement Health and Education Act (DSHEA 1994) permits for name explanations on dietary supplements. The FDA has centered on progressing shopper labeling data and requirement of DSHEA rules. A investigate venture pointed to get it customer mindfulness of dietary claims on dietary supplements and evaluate industry compliance with labeling necessities. The think about included 34 members, with 88% of ladies being recognizable with wholesome claims. The majority of items had labeling steady with later controls, with 65% of noncompliant items having inadequate disclaimers. [6]

Calcium discrepancies found in previous studies and their implications:

Calcium is pivotal for human wellbeing, particularly in anticipating and treating osteoporosis. Be that as it may, excessive calcium admissions can increment cardiovascular malady dangers. This article audits the wellbeing benefits, costs, and results of calcium

supplementation on osteoporosis, cardiovascular occasions, kidney stones, and other illnesses. It proposes cautious medicine and thought of person dangers. Advance studies are required to create strong suggestions. [7]

Calcium content determination:

Techniques used to determine the calcium content are spectrophotometer [8], Atomic Absorption Spectrometry (AAS), Inductively Coupled Plasma Mass Spectrometry (ICP-MS), Complexometric Titration, Flame Atomic Emission Spectroscopy (FAES), X-Ray Fluorescence (XRF), Colorimetric Methods can be used.

Why complexometric titration?

Complexometric titration is commonly employed in the determination of calcium content for several reasons:

This specificity reduces interference from other particles that will be display within the sample, resulting in exact judgments of calcium substance.

Complexometric titration is versatile and suitable for industries requiring calcium substance assurance for quality control or administrative compliance, as it can be applied to various sample frameworks.

Complex titrations accurately determine calcium content due to established stoichiometry between EDTA and calcium ions, allowing accurate calculation of calcium concentration based on titrant volume. [9]

Complex titrations are cost-effective and less expensive than other instrumental methods, making them an attractive option for laboratories with limited budgets.

Complex titration methods are widely standardized across industries and regulatory agencies, ensuring consistency and comparability of results between different laboratories through standard and procedural references.

RESEARCH AND METHODOLOGY

Selection criteria for multivitamin brands

The responsibility of examining the effects of multivitamin/mineral supplements on both healthy populations and those with chronic disease was assigned to the 2010 Dietary Guidelines Advisory Committee. Five basic criteria were used to judge the evidence that the committee used to prepare its conclusions: quality, consistency, quantity, clinical impact, and generalizability. The committee came to the conclusion that there wasn't enough data to prescribe multivitamins and minerals for the majority of healthy people. However, the committee also recognized the importance of some additional minerals, such iron, folic acid, and vitamin B-12, for populations that are at risk. The majority of the research's referenced studies, adhered to the traditional, comprehensive, and oversimplified definition of a multivitamin/mineral supplement, which is defined as one that contains three or more vitamins and minerals, either alone or in combination. [10]

Sample preparation

For solid samples, precisely weigh 0.5 g of the material into a conical flask or small beaker. Then, add 20 mL of diluted hydrochloric acid, and let the material dissolve completely—this could take a few minutes. Using a diluted sodium hydroxide solution, neutralize the unreacted acid until the solution's pH approaches 7 (as indicated by the pH indicator paper). After transferring the mixture to a 100 mL volumetric flask, top it up with distilled water.

Complexometric Titration procedure

1. Fill a conical flask with 10 mL of the sample solution using a pipette.
2. Pour in 20 mL of EDTA solution (0.05 mol L−1).
3. Add 1 mL of Eriochrome Black T indicator solution, 50 mL of distilled water, and 10 mL of ammonia buffer.
4. Use the standard 0.025 molL−1 magnesium chloride solution to titrate the sample until a persistent pink color is visible.

Calibration and Standardization

1. Transfer 10 ml of the EDTA solution via pipetting into a conical flask.
2. Add 1 mL of the Eriochrome Black T indicator solution and 10 mL of the ammonia buffer solution.
3. Titrate the magnesium chloride solution and EDTA until the endpoint is attained, which is a permanent shift in color from blue to pink.
4. After figuring out the magnesium chloride solution's average titre, figure out how many moles were utilized.

5. Determine the concentration of your EDTA solution using the Mg2+:EDTA ratio of 1:1. [11]
6- Experimental setup

Materials

This study utilized the following:

Chemicals: Analytical grade calcium chloride ($CaCl_2$), sodium hydroxide (NaOH), hydrochloric acid (HCl), magnesium chloride (mgcl2), ammonium chloride (NH4Cl) ethylenediaminetetraacetic acid (EDTA), Eriochrome black-T indicator, and distilled water.
Equipment: Analytical balance, burette, pipette, flask, measuring cylinder, volumetric flask(250ml), beaker, pH meter

Precautions

Wear rubber gloves and take precautions when handling the highly corrosive concentrated ammonia solution needed to prepare the indicator and buffer solutions.
A certain amount of ammonia gas will be released by the buffer, indicator, and Titration solution. If inhaled in large quantities, this gas may be hazardous. Use a fume-hood or a well-ventilated workspace.

Result

Data collection protocols
For each of the five chosen multivitamin brands, a triplicate Complexometric Titration analysis was conducted. The average measured calcium content for each brand was then determined (in milligrams per serving). Brand names are not published in this research for reasons of confidentiality. Table 2 displays the outcomes.

Table 2: Measured Calcium Content of Analyzed Multivitamin Brands

Brand ID	Labeled Calcium Content (mg)	Measured Calcium Content (mg)	Percentage of Labeled Value
1	80	73.66	92.08%
2	327	310.33	94.90%
3	500	373.00	74.60%
4	500	383.00	76.60%
5	500	400	80.00%

Comparison of Labeled and Measured Calcium Content

The results in Table 2 reveal variations in the measured calcium content compared to the labeled amounts on the multivitamin brands. While some brands (e.g., Brand 1 and Brand 2) exhibited good agreement between labeled and measured values (within 10%), others showed significant discrepancies. Brands 3, 4, and 5, for example, contained substantially less calcium than the labeled amount. [12]

Statistical analysis of data step by step

The Complexometric Titration of five different brands were performed three times. The moles of calcium were calculated, and the results showed that sample 1 contained 73.66 mg of calcium, sample 2 contained 310.33 mg of calcium, sample 3 contained 373 mg of calcium, sample 4 contained 383 mg of calcium, and sample 5 contained 400 mg of calcium, respectively. However, all samples contained the specified amount of calcium listed on the labels of the brands: 80mg in sample 1, 327mg in sample 2, 500mg in sample 3, 500mg in sample 4 and 500mg in sample 5. There are certain variations in calcium content in labels by comparing them to our calculated results, which are approximately 92.075% in sample 1, 94.902% in sample 2, 74.6% in sample 3, 76.6% in sample 4, and 80% in sample 5. Despite, this was not matched with our calculated results. Every element included on the label, including the claimed amount of calcium, needs to be authentic and accurate. For instance, a doctor might give a patient a prescription for a drug that, according to the label, contains 500 mg of active ingredient, but that amount may vary, making the drug ineffective for the patient's needs.

Every brand should make sure that each ingredient is used in the formulation in the amount specified on the label. [13]

Summary of Titration findings

The observed variations in measured calcium content highlight potential concerns regarding the accuracy of labeling in some multivitamin brands. Consumers rely on the information on product labels to make informed decisions about their nutrient intake. Inaccuracies in calcium content labeling can lead to consumers unknowingly consuming less calcium than intended, potentially increasing their risk of calcium deficiency and associated health problems.

Our findings are consistent with previous research using Complexometric Titration and other analytical techniques, which have reported similar discrepancies between labeled and measured calcium content in multivitamins.

1. Inconsistent mixing practices during manufacturing
2. Degradation of calcium compounds over time
3. Limitations of analytical methods

Discussions

Public Health Implications

Inaccurate labeling of calcium content in multivitamins poses a public health concern. Individuals who rely on multivitamins as a primary source of calcium may be unknowingly consuming insufficient amounts, potentially leading to:

1. Increased risk of osteoporosis and fractures, particularly for populations with higher calcium requirements (children, adolescents, older adults)
2. Muscle cramps
3. Dental problems

Recommendations

Based on these findings, we recommend the following:

Stricter regulations and enforcement: Regulatory bodies should implement stricter measures to ensure the accuracy of labeling information on multivitamin supplements, including calcium content.

Improved quality control practices: Manufacturers should implement robust quality control procedures throughout the production process to minimize variations in calcium content within multivitamin formulations.

Consumer awareness: Consumers should be aware of potential limitations of multivitamins as a sole source of calcium and prioritize a balanced diet rich in calcium-containing foods like dairy products, leafy green vegetables, and fortified foods.

Interpretation of results or conclusion

This study employed Complexometric Titration to evaluate the accuracy of labeled calcium content in five commercially available multivitamin brands. The analysis revealed variations in measured calcium content across the brands. While some brands demonstrated good agreement between labeled and measured values (within 10%), others exhibited significant discrepancies. The measured calcium content ranged from X mg to Y mg (representing Z% to W% of labeled values). Notably, a concerning proportion of brands contained less calcium than the labeled amount.

These findings raise concerns about the reliance on multivitamins to meet the recommended daily intake (RDI) of calcium. Consumers who depend solely on multivitamins for calcium intake may be unknowingly consuming insufficient amounts, potentially increasing their risk of calcium deficiency and associated health problems, such as osteoporosis and fractures.

The observed variations highlight the importance of stricter regulations and improved quality control measures to ensure accurate labeling of calcium content in multivitamin products. Consumers should also be aware of the limitations of multivitamins as a sole source of calcium and prioritize a balanced diet rich in calcium-containing foods for optimal bone health. Further research with a larger and more diverse sample size could provide even more robust insights into the accuracy of calcium labeling practices across the multivitamin industry.

References

Shlisky, J., Mandlik, R., Askari, S., Abrams, S., Belizan, J. M., Bourassa, M. W., Cormick, G., Driller-Colangelo, A., Gomes, F., Khadilkar, A., Owino, V., Pettifor, J. M., Rana, Z. H., Roth, D. E., & Weaver, C. (2022). Calcium deficiency worldwide: prevalence of inadequate intakes and associated health outcomes. *Annals of the New York Academy of Sciences*, *1512*(1), 10–28. https://doi.org/10.1111/nyas.14758

Lashkari, Cashmere. (2021, March 18). Calcium Deficiency Causes. News-Medical. Retrieved on May 26, 2024 from https://www.news-medical.net/health/Calcium-Deficiency-Causes.aspx.

Optimal calcium intake. (1994). NIH consensus statement, 12(4), 1–31. https://pubmed.ncbi.nlm.nih.gov/7599655/#:~:text=Recommended%20daily%20intake%20for%20men,needed%20for%20this%20age%20group.

Joanna Kozak, Alan Townshend, Paul Worsfold, Colin Poole, Alan Townshend, Manuel Miró, Titrimetry | Overview☆, Encyclopedia of Analytical Science (Third Edition),Academic Press,2019, https://doi.org/10.1016/B978-0-12-409547-2.14419-1. (https://www.sciencedirect.com/science/article/pii/B9780124095472144191)

George T, Brady MF. Ethylenediaminetetraacetic Acid (EDTA) [Updated 2023 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK565883/

Meer, M., Misner, S., & Meer, R. (2005). Labeling of Dietary Supplements: Consumer Awareness and Industry Compliance. Journal of Nutraceuticals, Functional & Medical Foods, 4(3–4), 29–44. https://doi.org/10.1300/J133v04n03_03

Li, K., Wang, X. F., Li, D. Y., Chen, Y. C., Zhao, L. J., Liu, X. G., Guo, Y. F., Shen, J., Lin, X., Deng, J., Zhou, R., & Deng, H. W. (2018). The good, the bad, and the ugly of calcium supplementation: a review of calcium intake on human health. Clinical interventions in aging, 13, 2443–2452. https://doi.org/10.2147/CIA.S157523

Xiao-Dong Li, Qing-Zhou Zhai, "Spectrophotometric Determination of Calcium with Dibromo-p-methylsulfonazo", Journal of Chemistry, vol. 2020, Article ID 9232385, 4 pages, 2020. https://doi.org/10.1155/2020/9232385

Zhai, J., & Bakker, E. (2016). Complexometric titrations: new reagents and concepts to overcome old limitations. Analyst, 141(14), 4252-4261. https://doi.org/10.1039/C6AN00538A

Comerford, K. B. (2013). Recent developments in multivitamin/mineral research. Advances in nutrition, 4(6), 644-656. https://doi.org/10.3945/an.113.004523 https://www.canterbury.ac.nz/content/dam/uoc-main-site/documents/pdfs/d-other/Determination-of-Total-Calcium-and-Magnesium-Ion-Concentration.pdf

Javed, A., & Saif, N. Preferences of Multinational & National Brands in Health Care. https://core.ac.uk/download/pdf/234624923.pdf

National Institutes of Health. Office of Dietary Calcium Supplements. https://ods.od.nih.gov/factsheets/CalciumHealthProfessional/.