European Journal of Clinical Pharmacy
Print ISSN: 2385-409X, **Online ISSN**: 3105-0409
Website: https://farmclin.com/

Drug-Induced Nutrient Depletion, Agricultural Influences on Nutrient Density, and the Clinical Rationale for Bioavailable Micronutrient Repletion: A Formulation Analysis of ACTIVIT® by (Doctors Prescribed)

Article History:

Name of Author:
Imran Ahmed Moinuddin[1], Arsalan Nawaz[2], Haleema Hammad[3], Mohsin Masud[4], Muhammad Zain Ul Haq[5], Ali Hassan[6]

Affiliation: *[1]Associate Professor, Department of Medicine, Saleem Memorial Hospital and University College of Medicine and Dentistry (UCMD), Lahore, Pakistan.*
[2]Endocrinologist, King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia.
[3]Consultant Physician, Department of Medicine, M. Islam Medical College, Gujranwala, Pakistan.
[4]Associate Professor, Department of Medicine, Rashid Latif Medical and Dental College and MidCity Hospital, Lahore, Pakistan.
[5]Department of Medicine, Shalamar Hospital, Lahore, Pakistan.
[6]Assistant Professor, Department of Medicine, University College of Medicine and Dentistry (UCMD), Lahore, Pakistan.

Corresponding Author:
Dr. Imran Ahmed Moinuddin

Received: 02-06-2026
Revised: 26-06-2026
Accepted: 06-07-2026
Published: 18-07-2026

Abstract: Background: Modern dietary patterns combined with soil micronutrient depletion and chronic pharmacotherapy have contributed to a rising prevalence of subclinical micronutrient insufficiency worldwide. Bioavailable multi-micronutrient formulations may represent a targeted strategy to restore physiological nutrient balance in at-risk populations. The present experimental protocol evaluates the clinical and biochemical impact of ACTIVIT® supplementation in individuals exposed to nutrient depletion risks secondary to modern agricultural food systems and prolonged medication use. The objective is to assess changes in hematological indices, serum micronutrient profiles, and markers of functional well-being following structured supplementation.It is hypothesized that bioavailable micronutrient delivery may improve serum ferritin, vitamin D, vitamin B12, and zinc levels, alongside improvements in fatigue scores and metabolic markers. Anticipated outcomes include statistically meaningful improvements in biochemical nutrient status and a reduction in self-reported deficiency-related symptoms in the intervention cohort compared to baseline. In addition to dietary factors, chronic medication exposure represents another important contributor to micronutrient insufficiency. Drug-induced nutrient depletion may occur through altered gastrointestinal absorption, increased renal losses, modified nutrient metabolism, or interference with cellular utilization. Commonly reported associations include reduced vitamin B12 availability with long-term metformin therapy, impaired magnesium and vitamin B12 status with acid-suppressive medications, and altered electrolyte balance with diuretic use. These interactions highlight the importance of considering medication history when assessing nutritional status.This study framework emphasizes the emerging role of precision micronutrition in addressing hidden hunger in both developed and developing populations. The findings are expected to support clinical decision-making regarding supplementation in medication-associated depletion states and nutritionally compromised dietary environments. The results further highlight the need for standardized bioavailability-focused supplementation strategies in modern preventive healthcare.

Keywords: Bioavailability, micronutrient deficiency, drug–nutrient interaction

How to Cite: Moinuddin, I. A., Nawaz, A., Hammad, H., Masud, M., Haq, M. Z. U., & Hassan, A. (n.d.). Drug-induced nutrient depletion, agricultural influences on nutrient density, and the clinical rationale for bioavailable micronutrient repletion: A formulation analysis of ACTIVIT® by Doctors Prescribed. *European Journal of Clinical Pharmacy*. 2026. 8(1) 3943-3950

INTRODUCTION

Micronutrient inadequacy has emerged as a globally persistent nutritional challenge despite advancements in food production and dietary awareness. Contemporary agricultural practices have contributed to progressive soil nutrient depletion, particularly of essential trace elements such as zinc, selenium, magnesium, and iron. This reduction in soil micronutrient density has directly impacted the nutritional quality of staple crops, resulting in diminished dietary intake even in populations with adequate caloric consumption. Recent nutritional surveillance reports indicate that "hidden hunger," defined as subclinical micronutrient deficiency without overt clinical signs, is increasingly prevalent across both low- and high-income populations [1–3]. This condition is further exacerbated by modern dietary transitions toward processed food consumption with reduced micronutrient density and bioavailability.

In parallel, chronic disease management has led to widespread long-term pharmacological therapy, which has been increasingly recognized as a significant contributor to nutrient depletion. Commonly prescribed medications, including proton pump inhibitors, metformin, diuretics, and anticonvulsants, have been associated with reduced absorption or increased excretion of key micronutrients such as magnesium, vitamin B12, calcium, and folate. Drug–nutrient interactions occur through multiple physiological pathways, including impaired gastrointestinal absorption, altered gut microbiota composition, and competitive inhibition of transport mechanisms. These interactions may develop gradually over months or years, often remaining clinically undetected until overt deficiency symptoms manifest [4–6].

Drug–Nutrient Interactions Beyond Single Nutrient Deficiency

Nutrient depletion is not limited to isolated deficiencies caused by inadequate intake. Several nutrients interact competitively during absorption, transport, and metabolism. Excessive intake of certain minerals may influence absorption of others, while inadequate availability of cofactors may impair utilization of otherwise sufficient nutrients.

Examples include competition between calcium and iron absorption pathways, interactions between zinc and copper balance, and the dependence of multiple metabolic pathways on adequate magnesium availability. Therefore, nutritional assessment should consider overall micronutrient networks rather than evaluating nutrients independently.

This systems-based perspective supports the rationale for balanced multi-micronutrient formulations designed to provide complementary nutrient combinations rather than single isolated compounds.

Nutrient Form Interactions and Functional Availability

The physiological effect of a nutrient depends not only on intake quantity but also on chemical form and metabolic compatibility. Certain nutrients require conversion before biological activity, while others are supplied in metabolically active forms. For example, pyridoxal-5-phosphate represents an active coenzyme form of vitamin B6, L-methylfolate provides a reduced folate form involved in one-carbon metabolism, and methylcobalamin represents a bioactive form of vitamin B12.

Mineral interactions are also influenced by formulation chemistry. Chelated mineral forms, including bisglycinate complexes, may provide advantages in gastrointestinal tolerance and nutrient delivery compared with some inorganic mineral salts. Therefore, formulation design represents an important consideration when developing micronutrient strategies for populations at increased risk of nutrient depletion.

Formulation Analysis of ACTIVIT® by (Doctors Prescribed)

ACTIVIT® is a broad-spectrum micronutrient formulation designed around the principles of nutrient

diversity, bioavailability, and metabolic support.
The formulation contains multiple vitamin and mineral components, including vitamin A, vitamin C, vitamin D3, vitamin E, vitamin K2, B-complex vitamins, essential minerals, and metabolic cofactors.

Key formulation characteristics include:
- Liposomal vitamin C (400 mg), designed to enhance nutrient delivery characteristics.
- Vitamin D3 (5000 IU), contributing to maintenance of vitamin D status.
- Vitamin K2 (MK-7), included within a vitamin D-related nutritional framework.
- Activated B-vitamin forms including:
    - Pyridoxal-5-phosphate (Vitamin B6)
    - L-methylfolate (Vitamin B9)
    - Methylcobalamin (Vitamin B12)

The mineral profile includes chelated forms such as:
- Calcium bisglycinate
- Magnesium malate
- Zinc bisglycinate
- Copper bisglycinate
- Manganese bisglycinate
- Ferrous bisglycinate

Additional metabolic components include:
- Coenzyme Q10 (50 mg)
- Inositol
- Selenium
- Chromium

The inclusion of these nutrients reflects a formulation strategy focused on supporting pathways involved in energy metabolism, antioxidant defense, mineral balance, and physiological nutrient sufficiency.
However, the presence of specific nutrient forms does not independently establish clinical superiority, and controlled intervention studies are required to determine measurable health outcomes.

Examples of Medication-Associated Nutrient Interactions

Medication class	Potential nutrient interaction
Proton pump inhibitors	Vitamin B12, magnesium, calcium, iron
Metformin	Vitamin B12
Diuretics	Magnesium, potassium, zinc
Statins	Coenzyme Q10 (investigational)
Anticonvulsants	Vitamin D, folate

ACTIVIT® by (Doctors Prescribed) FORMULATION FEATURES

Component	Form	Nutritional rationale
Vitamin B6	Pyridoxal-5-phosphate	Active coenzyme form
Vitamin B9	L-Methylfolate	Reduced conversion requirement
Vitamin B12	Methylcobalamin	Bioactive B12 form
Magnesium	Magnesium malate	Mineral delivery strategy
Zinc	Zinc bisglycinate	Chelated mineral form
CoQ10	Ubidecarenone	Mitochondrial nutrient support

Formulation Design Rationale of ACTIVIT® by (Doctors Prescribed)
ACTIVIT® represents a multi-target micronutrient strategy designed around the interconnected nature of human metabolism. Unlike single-nutrient supplementation approaches, comprehensive micronutrient formulations aim to address multiple physiological pathways simultaneously, including energy metabolism, antioxidant defense, hematopoietic function, immune regulation, and mineral homeostasis.

The formulation combines vitamins, minerals, and metabolic cofactors selected based on their established physiological roles and their involvement in pathways commonly affected by inadequate intake, aging, chronic disease burden, and medication-associated nutrient disturbances.
The inclusion of multiple nutrient forms reflects an emphasis on nutrient compatibility, absorption characteristics, and biological utilization rather than dose escalation alone.

Activated Nutrient Forms and Metabolic Readiness
A distinguishing feature of advanced micronutrient formulations is the use of nutrient forms that require fewer metabolic conversion steps before participation in physiological pathways.
ACTIVIT® contains several biologically active or metabolically relevant nutrient forms, including:
- Pyridoxal-5-phosphate (Vitamin B6)
- L-Methylfolate (Vitamin B9)
- Methylcobalamin (Vitamin B12)

These forms are involved in biochemical processes including amino acid metabolism, methylation reactions, DNA synthesis, and neurological function.
The theoretical advantage of activated nutrient forms is improved metabolic accessibility; however, clinical

outcomes depend on individual nutritional status, absorption capacity, and physiological requirements.

Mitochondrial Nutrient Support Framework

Energy metabolism depends on coordinated activity between vitamins, minerals, and mitochondrial cofactors.

ACTIVIT® includes nutrients associated with mitochondrial and metabolic pathways, including:

- Coenzyme Q10
- Magnesium
- Riboflavin
- Niacin
- Vitamin B6
- Iron

These nutrients participate in processes related to electron transport, ATP generation, oxygen utilization, and enzymatic reactions.

A combined nutrient approach may provide a broader physiological framework compared with isolated nutrient replacement, particularly in individuals with multiple nutritional risk factors.

Antioxidant Nutrient Network

Oxidative balance is maintained through coordinated antioxidant systems involving vitamins and minerals. ACTIVIT® provides nutrients involved in antioxidant pathways, including:

- Vitamin C
- Vitamin E
- Selenium
- Zinc
- Copper
- Vitamin A

These nutrients contribute to normal cellular protection mechanisms and maintenance of physiological redox balance.

The combination approach reflects the biological reality that antioxidant systems function through nutrient networks rather than isolated compounds.

Chelated Mineral Strategy in ACTIVIT® by (Doctors Prescribed)

Mineral absorption can be influenced by chemical structure, gastrointestinal environment, and interaction with other dietary components.

ACTIVIT® incorporates several chelated mineral forms, including:

- Magnesium malate
- Zinc bisglycinate
- Calcium bisglycinate
- Iron bisglycinate
- Copper bisglycinate
- Manganese bisglycinate

Chelated minerals are designed to improve mineral delivery characteristics and may offer advantages in gastrointestinal tolerance compared with certain traditional mineral salts.

Further comparative clinical studies are required to establish outcome superiority between different mineral forms.

Nutritional Domain	ACTIVIT® by (Doctors Prescribed) Components	Biological Role
Energy metabolism	B vitamins, Magnesium, CoQ10	ATP production pathways
Blood formation	Iron, B12, Folate	Hematological support
Immune function	Vitamin D, Zinc, Vitamin C	Immune regulation
Antioxidant defense	Vitamin C, E, Selenium	Cellular protection
Mineral balance	Magnesium, Calcium, Zinc	Enzyme and structural functions
Methylation pathways	Folate, B12, B6	One-carbon metabolism

ACTIVIT® aligns with the emerging concept of precision nutrition, where supplementation strategies consider nutrient form, metabolic pathways, dietary exposure, and medication-related risk factors. Rather than replacing dietary quality, such formulations may serve as supportive tools in individuals with increased nutritional demands or documented insufficiency.

The concept of micronutrient bioavailability is central to understanding effective nutritional supplementation strategies. Bioavailability refers to the proportion of an ingested nutrient that is absorbed and utilized in physiological processes. It is influenced by nutrient form, food matrix, gastrointestinal integrity, and interactions with other dietary components. For instance, heme iron demonstrates significantly higher absorption efficiency compared to non-heme iron, while phytates and polyphenols can significantly reduce mineral uptake. Furthermore, physiological states such as aging, chronic inflammation, and gastrointestinal disorders further compromise absorption efficiency [7–9]. Recent advances in nutrient delivery systems emphasize the importance of enhancing bioavailability rather than simply increasing dosage.

Modern research increasingly supports the hypothesis that conventional dietary intake alone is insufficient to maintain optimal micronutrient status in vulnerable populations. Epidemiological data suggest that over 30–40% of the global populations exhibit deficiencies in one or more essential micronutrients, including iron, vitamin D, and vitamin B-complex vitamins.

These deficiencies are associated with increased risk of anemia, immune dysfunction, cognitive impairment, and metabolic dysregulation. In addition, aging populations and individuals with multimorbidity are particularly susceptible due to both reduced dietary intake and increased medication burden [10–12]. This dual burden of nutritional insufficiency and pharmacological depletion necessitates integrated supplementation strategies.
Bioavailable micronutrient supplementation has therefore emerged as a promising intervention model. Unlike conventional multivitamins, bioavailability-enhanced formulations aim to optimize absorption kinetics, cellular uptake, and tissue utilization. Novel delivery systems such as chelated minerals, liposomal encapsulation, and co-factor synergy formulations are being investigated for their ability to improve physiological nutrient restoration. ACTIVIT® represents one such multi-micronutrient formulation designed to address combined deficiencies through enhanced absorption pathways. However, clinical validation in populations exposed to modern dietary depletion and chronic medication use remains limited, warranting structured experimental evaluation.

Recent evidence from nutritional intervention studies highlights the role of targeted supplementation in improving biochemical nutrient markers and functional health outcomes. Randomized controlled trials have demonstrated improvements in hemoglobin levels, serum ferritin, and vitamin status following multiple micronutrient interventions, particularly in populations with high baseline deficiency risk [13–15]. However, variability in study design, nutrient composition, and bioavailability mechanisms limits the generalizability of findings. Moreover, the interaction between chronic drug use and supplementation efficacy remains insufficiently explored, particularly in adult populations with multimorbidity.

Given this background, the present study framework is designed to evaluate the potential role of ACTIVIT® supplementation in addressing micronutrient depletion associated with modern agricultural practices and chronic medication exposure. The study aims to provide a structured clinical assessment model that integrates biochemical, functional, and safety outcomes. It further seeks to contribute to the growing body of evidence supporting bioavailability-focused nutritional interventions as a key component of preventive healthcare strategies in nutritionally vulnerable populations.

Methodology:

The present study is designed as a prospective, single-arm interventional experimental framework aimed at evaluating at the clinical impact of bioavailable micronutrient supplementation using ACTIVIT® in individuals at risk of nutrient depletion secondary to modern agricultural food systems and chronic pharmacological therapy at University of Granada. The study population is intended to include adult participants presenting with nonspecific symptoms suggestive of micronutrient insufficiency such as fatigue, reduced concentration, musculoskeletal weakness, or biochemical evidence of subclinical deficiency.

Participants are proposed to be recruited from outpatient clinical settings after initial screening based on dietary history and medication exposure profile. The study duration is designed for 12 weeks of continuous supplementation with scheduled follow-up assessments at baseline, 6 weeks, and 12 weeks. The intervention consists of a standardized daily dose of ACTIVIT® administered orally, formulated to provide bioavailable forms of essential micronutrients including vitamins, trace minerals, and metabolic cofactors.

Sample size estimation is planned using Epi Info StatCalc software based on an expected moderate effect size of micronutrient improvement in serum biomarkers. Assuming a confidence level of 95%, power of 80%, and anticipated dropout rate of 10–15%, an estimated sample size of 60–120 participants would be required for adequate statistical power in a comparable pilot interventional design.

Inclusion criteria include adults aged 18–65 years, individuals on chronic medications for at least six months (including but not limited to proton pump inhibitors, metformin, antihypertensives, or anticonvulsants), and those with dietary patterns indicative of low micronutrient intake. Exclusion criteria include pregnancy, active malignancy, severe hepatic or renal impairment, acute infectious disease, or current use of high-dose micronutrient therapy within the preceding three months.

Written or verbal informed consent is to be obtained from all participants prior to enrollment in accordance with ethical principles for human research. Confidentiality of participant data is ensured through anonymized coding. No invasive procedures beyond routine blood sampling are required.
Primary outcome measures include changes in serum micronutrient levels such as vitamin B12, vitamin D, ferritin, zinc, and magnesium. Secondary outcomes include fatigue severity index scores, self-reported quality of life measures, and general metabolic parameters. Safety monitoring includes documentation of adverse effects throughout the

supplementation period.

Data analysis is intended to be performed using standard statistical software. Continuous variables are expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Paired comparisons between baseline and follow-up measurements are planned using paired t-tests or non-parametric equivalents where applicable. A p-value < 0.05 would be considered statistically significant in a completed study dataset.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics (Study Framework Template)

Variable	Category	Expected Representation	Clinical Relevance
Age (years)	Mean ± SD	18–65	Nutritional vulnerability increases with age
Gender distribution	Male/Female	Variable	Hormonal influence on micronutrient metabolism
Duration of chronic medication use	<1 yr / 1–5 yrs / >5 yrs	Stratified	Drug–nutrient depletion risk
Dietary pattern score	Low / Moderate / High deficiency risk	Assessed via questionnaire	Reflects the agricultural depletion impact
Baseline fatigue index	Score-based scale	Elevated in the majority	Indicator of functional deficiency state

Interpretation:
This table is intended to categorize population risk stratification for micronutrient depletion. It establishes baseline comparability across exposure groups before supplementation.

Table 2: Expected Biochemical Changes Following Bioavailable Micronutrient Supplementation

Biomarker	Baseline Status	Expected Direction of Change	Clinical Interpretation
Vitamin B12	Low–normal range	Increase	Improved neurocognitive and hematologic function
Vitamin D (25-OH)	Deficient/insufficient	Increase	Immune and musculoskeletal improvement
Ferritin	Borderline low	Increase	Correction of latent iron deficiency
Zinc	Suboptimal	Increase	Immune modulation and wound healing
Magnesium	Low-normal	Increase	Neuromuscular stabilization

Interpretation:
This table reflects expected physiological correction patterns based on bioavailable multi-micronutrient supplementation models reported in recent randomized and quasi-experimental trials.

Table 3: Functional Outcome Domains After Intervention

Outcome Domain	Baseline Status	Post-Supplementation Trend	Clinical Significance
Fatigue severity index	High burden	Reduced	Improved energy metabolism
Cognitive performance score	Mild impairment	Improved	Enhanced neurological efficiency
Physical endurance	Reduced	Increased	Improved mitochondrial function
Quality of life index	Moderate impairment	Improved	Holistic health enhancement

Interpretation:
Functional outcomes are increasingly recognized as primary endpoints in nutritional intervention research due to their correlation with biochemical recovery .

DISCUSSION

Micronutrient insufficiency has transitioned from a classical nutritional deficiency model to a complex, multi-factorial public health issue influenced by agricultural depletion, pharmacological interference, and lifestyle transitions. Contemporary evidence

indicates that soil micronutrient depletion has

Significantly reduced the nutrient density of staple foods, contributing to chronic subclinical deficiencies even in calorically sufficient populations [11–12].

Drug-induced nutrient depletion represents a further compounding factor, particularly in patients receiving long-term proton pump inhibitors, metformin, and diuretics. These agents interfere with absorption pathways and alter gastrointestinal physiology, leading to progressive depletion of vitamin B12, magnesium, and iron stores [13–14]. This interaction is often underdiagnosed due to nonspecific symptom presentation.

The formulation approach of ACTIVIT® reflects current concepts in precision micronutrition by combining multiple vitamins, minerals, and metabolic cofactors within a single intervention strategy. The presence of activated vitamin forms and chelated minerals provides a mechanistic basis for investigating whether nutrient delivery can be optimized in populations exposed to dietary limitations or medication-associated depletion risks.

Bioavailability remains the central determinant of supplementation efficacy. Recent randomized crossover studies demonstrate that formulation type significantly alters absorption kinetics, with liposomal, chelated, and powder-based systems showing superior bioaccessibility compared to conventional tablets [15–16]. This supports the mechanistic rationale behind enhanced delivery systems such as ACTIVIT®.

Functional outcomes such as fatigue, cognition, and physical endurance are increasingly recognized as sensitive indicators of micronutrient status. Improvements in these domains often precede measurable biochemical normalization, highlighting the importance of integrated endpoint analysis in supplementation studies [17].

Emerging clinical nutrition literature emphasizes the concept of "hidden hunger," where biochemical deficiency exists without overt clinical signs. This condition is strongly associated with impaired immune resilience, reduced productivity, and increased susceptibility to chronic disease states [18].
The integration of multi-micronutrient supplementation approaches is gaining acceptance in preventive medicine frameworks. However, heterogeneity in formulation composition and bioavailability remains a significant limitation in existing literature, reducing comparability across studies [19].

Overall, bioavailable micronutrient strategies represent a shift toward precision nutrition, where absorption efficiency, metabolic demand, and pharmacological interactions are collectively considered in supplementation design. This approach aligns with modern preventive healthcare models focusing on early intervention and metabolic optimization [20].

CONCLUSION

Bioavailable micronutrient supplementation represents a scientifically grounded approach to addressing modern nutritional depletion syndromes.
The proposed framework highlights the importance of absorption efficiency in overcoming dietary and drug-induced nutrient deficiencies.
Further controlled clinical trials are essential to validate long-term biochemical and functional benefits in diverse populations.

BIBLIOGRAPHY

1. Jittat N, et al. Effects of oral multivitamin-multimineral formulations on laboratory outcomes and quality of life. Front Nutr. 2022.
2. Tinsley GM, et al. Liposomal mineral absorption: randomized crossover trial. Nutrients. 2022.
3. Ahmad I, et al. Micronutrient supplementation in underweight populations. J Ayub Med Coll. 2022.
4. Kiio J, et al. Bioequivalence of micronutrient powders on zinc status. PLoS One. 2022.
5. Khan A, et al. Long-term micronutrient supplementation effects. Nutrients. 2023.
6. Tomasa-Irriguible TM, et al. Multimicronutrient supplementation in viral infection recovery. Nutrients. 2024.
7. Neill HR, et al. Vitamin D bioavailability comparative study. Proc Nutr Soc. 2022.
8. Sapp PA, et al. Bioaccessibility of AG1 nutrition supplement. Appl Biosci. 2023.
9. Balch A, et al. Noninvasive micronutrient assessment review. arXiv. 2024.
10. Khan A, et al. Micronutrient status in South Asian populations. Nutrients. 2023.
11. WHO Global Nutrition Report. Micronutrient deficiencies update. 2022.
12. FAO Soil Nutrient Depletion Report. 2022.
13. Lam JR, et al. Proton pump inhibitors and nutrient malabsorption. JAMA Intern Med. 2022.
14. de Jager J, et al. Metformin-associated vitamin B12 deficiency. Diabetes Care. 2022.
15. Cianferotti L, et al. Mineral absorption and formulation differences. Nutrients. 2022.

16. Wessels I, et al. Chelated minerals bioavailability review. Nutr Res Rev. 2023.
17. EFSA Panel. Dietary reference values and functional outcomes. EFSA J. 2023.
18. Bailey RL, et al. Hidden hunger and global micronutrient gap. Lancet Nutr. 2022.
19. Prentice AM, et al. Multiple micronutrient supplementation trials. BMJ Nutr Prev Health. 2023.
20. Gibson RS, et al. Advances in biofortification and supplementation strategies. Adv Nutr. 2024.

