

# Evaluation of micronutrient adequacy in adult enteral formulas in Türkiye: a comparison with DRI, ESPEN, and National Guideline (TUBER-2022)

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## ABSTRACT

**Objective:** Enteral nutrition (EN) is a cornerstone of nutritional support for patients unable to meet their dietary needs orally, yet concerns remain regarding the adequacy of micronutrient provision in commercial enteral formulas. The aim of the study is to evaluate the micronutrient content of commonly used adult enteral formulas in Türkiye by comparing their composition with the recommendations provided in international and national guidelines.

**Methods:** Thirty-eight commercially available adult enteral formulas, encompassing standard, immune-modulating, and disease-specific types were analyzed. The micronutrient content was calculated based on the labelled values and subsequently adjusted for daily energy intakes of 1500 and 1800 kcal. These values were then compared with Dietary Reference Intakes (DRIs), ESPEN micronutrient guidelines, and TUBER-2022 recommendations.

**Results:** At a 1500 kcal/day EN intake, 89.1% of the formulas (33/37) failed to meet the recommended intake for vitamin K, 86.5% (32/37) for vitamin D, and 94.6% (35/37) for magnesium based on DRI and ESPEN guidelines. Additionally, 37.8% (14/37) of the formulas did not meet the iron requirement specifically for females according to DRI and ESPEN recommendations. According to ESPEN's recommendations for high demand, all formulas were found to be insufficient in multiple micronutrients, including vitamins A, D, E and B-complex vitamins, as well as iron, zinc, selenium, chromium and molybdenum. Furthermore, one immune-modulating formula exceeded the tolerable upper intake levels for five micronutrients (folic acid, calcium, magnesium, zinc, and manganese) according to both the DRI and the TUBER-2022.

**Conclusion:** Commonly used enteral formulas in Turkey may inadequately supply essential micronutrients, particularly to vulnerable populations with increased requirements. These findings emphasize the need for routine clinical monitoring, individualized supplementation strategies and reformulation of products, especially with regard to vitamin D and magnesium content, to align with ESPEN's higher intake recommendations.

**Keywords:** enteral nutrition, micronutrient, DRI, ESPEN, TUBER

## Introduction

Enteral nutrition (EN) is a key part of nutritional management for patients who cannot meet their dietary requirements through oral intake, but who have an

intact and functional gastrointestinal tract. EN plays a critical role in preserving gut integrity, supporting immune function and mitigating the risks of malnutrition in various clinical contexts.<sup>1</sup> The increasing variety and range of commercial enteral formulas provide clinicians

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with options tailored to specific patient needs, including standard, immune-modulating and disease-specific formulations.<sup>2</sup>

Enteral formulas are typically developed based on the Dietary Reference Intakes (DRIs). They are designed to deliver essential nutrients—including macronutrients, micronutrients, and antioxidants—to meet the daily nutritional needs of diverse patient populations, ranging from critically ill, hypermetabolic individuals to stable patients receiving long-term home enteral nutrition.<sup>3</sup> However, DRIs primarily represent reference intake values intended for healthy individuals and general population groups.<sup>4</sup> Despite the widespread use of enteral formulas, concerns persist regarding whether their micronutrient content adequately meets the nutritional demands outlined by current clinical guidelines.

Micronutrients, including vitamins, minerals and trace elements, are essential for many physiological processes, including immune defense, enzymatic activity and metabolism. Both micronutrient deficiencies and excesses may adversely affect clinical outcomes, particularly in vulnerable populations such as older adults, individuals with chronic diseases.<sup>5,6</sup> Patients receiving prolonged enteral nutrition are particularly susceptible to micronutrient imbalances, which can result in significant clinical complications, including deficiencies and toxicities.<sup>7-9</sup>

To ensure optimal patient care, it is essential to systematically assess the micronutrient profiles of commercially available enteral formulas by comparing them with established international and national dietary guidelines.<sup>10</sup> Key reference standards include the Dietary Reference Intakes (DRIs)<sup>11</sup>, the micronutrient

guideline of the European Society for Clinical Nutrition and Metabolism (ESPEN)<sup>5</sup>, and the Turkish Nutrition Guideline (TUBER-2022).<sup>12</sup> The DRIs<sup>11</sup> provide nutrient intake recommendations primarily based on healthy populations and serve as a general reference for adequate nutrient consumption. In contrast, ESPEN guideline<sup>5</sup> focus specifically on clinical nutrition, offering tailored recommendations for patients with diverse medical conditions and metabolic demands. TUBER-2022<sup>12</sup>, as a national guideline, integrates local nutritional considerations and population-specific data to guide clinical nutrition practices in Türkiye. These standards provide recommendations for appropriate micronutrient intake in clinical nutrition practice.

In Türkiye, the use of enteral nutrition formulas is steadily increasing; however, there is limited data available regarding their micronutrient adequacy compared to international and national guidelines. This study aims to evaluate the micronutrient contents of commonly used adult enteral formulas in Türkiye and compare them with the recommendations of DRI, ESPEN, and TUBER-2022, thereby providing clinicians with essential information to guide formula selection and optimize nutritional management.

## Methods

This study evaluated 38 adult EN formulas produced by three different manufacturers and available commercially in Türkiye. The formulas were categorized into three groups: 21 standard EN formulas, six immune-modulating formulas, and 11 disease-specific formulas (for diabetes, pulmonary disease, renal disease, and malabsorption). Nutritional data were extracted from product labels available on official websites or technical documents provided by manufacturers.

In this study, nutrient reference values were obtained from several authoritative sources to ensure comprehensive assessment. The DRI<sup>11</sup> provided Recommended Dietary Allowance (RDA), which represents the average daily intake sufficient to meet the nutrient requirements of nearly all healthy individuals, and Tolerable Upper Intake Level (UL), indicating the maximum daily intake unlikely to cause adverse health effects. The ESPEN<sup>5</sup> supplied minimum and maximum nutrient requirements, defining safe intake ranges applicable in clinical nutrition settings. Additionally, the TUBER-2022<sup>12</sup> offered Adequate Intake (AI), recommended when RDA values are not established, along with UL values to identify upper intake limits.

### Main Points

- The majority of adult enteral formulas available in Turkey do not meet the recommended intake levels for key micronutrients, particularly vitamin D, vitamin K, magnesium, and iron.
- In comparison with the higher intake recommendations set out by ESPEN, a more extensive insufficiency of micronutrients was identified.
- These findings emphasise the necessity of revising product formulations and strengthening clinical strategies to align with international and national nutritional standards.

The micronutrient content of each product was calculated based on the labelled values and standardized to daily energy intakes of 1500 and 1800 kcal/day.<sup>10,13</sup> These values were then compared with the recommendations of the DRIs<sup>11</sup>, ESPEN micronutrient guideline<sup>5</sup>, and the TUBER-2022.<sup>12</sup> The average micronutrient levels were then assessed, and nutrients that did not meet the recommended levels were examined in detail across all enteral formulas.

Data analysis was performed using RStudio software (version 2022.07.1, RStudio PBC, Boston, MA, USA). Continuous variables were presented as median (minimum–maximum). Micronutrients that did not meet the recommended intake thresholds were identified and analyzed in more detail across formula categories. This study was designed as a descriptive analysis aiming to compare micronutrient contents with established guidelines; therefore, no statistical hypothesis testing was conducted.

## Results

The micronutrient contents of the evaluated enteral formulas at a 1500 kcal intake, along with the corresponding reference values and tolerable upper intake levels based on DRI, ESPEN, and TUBER-2022 guidelines, are summarized in Table 1. Additionally, Figure 1 illustrates the percentages of micronutrient provision relative to the recommended daily intake levels.

According to the DRI, the enteral formulas provided 56.10–67.32% of the recommended daily potassium intake, 59.46–71.36% of chloride, 67.17–80.61% of magnesium, 76.79–92.14% of sodium, and 81.20–97.43% of vitamin K when administered at energy levels of 1500–1800 kcal per day. Eleven other micronutrients met or exceeded daily requirements and remained well below the established tolerable upper intake levels, indicating a safe intake range for these nutrients.

Based on ESPEN guidelines, the formulas provided 62.58–75.10% of the recommended daily vitamin D intake, 66.39–79.66% of the recommended daily iron intake, and 81.20–97.44% of the recommended daily vitamin K intake, all at the same energy levels. Other micronutrients were supplied in adequate amounts.

When evaluated in reference to the TUBER-2022 guidelines, the formulas provided 54.50–65.40% of the recommended potassium intake and 57.59–69.11% of the recommended sodium intake. Other micronutrients met

or exceeded daily requirements while remaining safely below the upper intake limits, suggesting no potential risk of excessive intake.

However, when evaluated according to the higher intake recommendations outlined in ESPEN guidelines, the enteral formulas were insufficient in providing several key micronutrients at a 1500 kcal/day intake. These included vitamins A, D, and E, B-complex vitamins (thiamine, riboflavin, niacin, vitamin B6, biotin, folic acid, and vitamin B12), as well as the minerals iron, zinc, selenium, chromium, and molybdenum (Figure 2).

Detailed evaluation of vitamin D, vitamin K, iron, and magnesium contents at both 1500 kcal and 1800 kcal intake levels revealed persistent inadequacies across most formulas, as presented in Figure 3. With the exception of one immune-modulating formula, the remaining products failed to provide sufficient vitamin D intake according to ESPEN recommendations at 1500 kcal/day. Additionally, based on DRI and TUBER-2022 criteria, 45.9% (17 out of 37) of the enteral formulas were inadequate in meeting the daily vitamin D requirement at this energy level.

Although 81.1% (30 out of 37) of the formulas met the vitamin K requirement according to TUBER-2022 guidelines, adequacy rates significantly declined when compared to the standards of DRI and ESPEN, with only 10.8% (4 out of 37) meeting the recommended levels. In contrast, 89.1% (33 out of 37) of the formulas failed to meet the vitamin K requirements according to DRI and ESPEN guidelines (Figure 3).

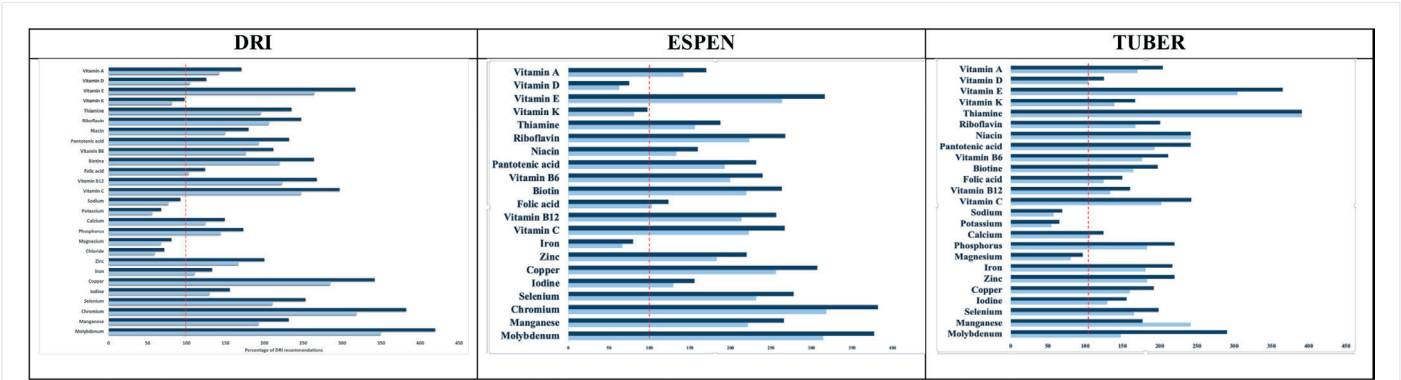
Regarding magnesium, only one immune-modulating formula (2.6%) met the minimum requirements defined by both DRI and TUBER-2022 at an intake of 1500 kcal/day.

All enteral formulas provided sufficient iron at 1500 kcal/day for males based on both DRI and TUBER-2022 recommendations. However, 37.8% (14 out of 37) of the formulas did not meet the iron requirement for females according to DRI and the lower reference range of ESPEN. Furthermore, one formula achieved the higher iron intake recommended by ESPEN for this energy level (Figure 3).

Finally, among the 38 evaluated formulas, one immune-modulating formula exceeded the UL for five micronutrients (folic acid, calcium, magnesium, zinc, and manganese) according to both DRI and TUBER-2022 guidelines.

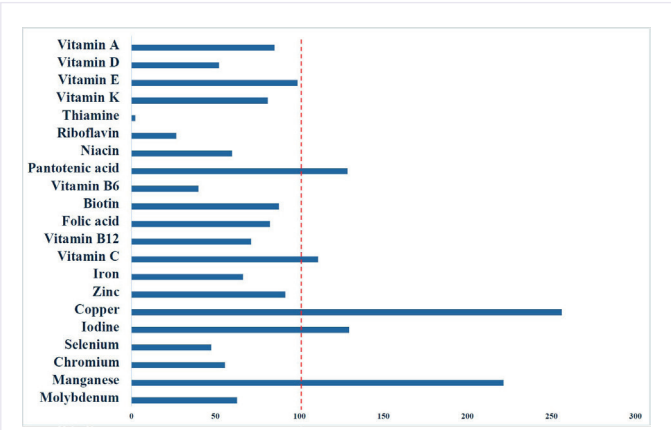
Table 1. Micronutrient Content of Enteral Formulas at 1500 kcal/day Compared to Recommendations from DRIs, ESPEN Guidelines, and TUBER-2022.											
	Overall (n=38)	Standard formula (n=21)	Immun-modulating formula (n=6)	Disease-specific formula (n=11)	DRI		ESPEN			TUBER	
					RDA (m/f)	UL	Min-max	High	AI	UL	UL
Vitamin A (mcg)	1230 (280-1792)	1230 (280-1650)	1444 (600-1792)	1230 (675-1769)	900/700	3000	900-1500	1500	750/650	3000	3000
Vitamin D (mcg)	14.8 (9.3-57.0)	15.0 (9.7-22.5)	10.0 (9.3-57.0)	14.0 (10.2-23.2)	15	100	25	30	15	100	100
Vitamin E (mg)	28.1 (18.8-229.8)	24.8 (18.8-32.2)	44.2 (25.0-229.8)	29.0 (19.5-207.2)	15	1000	15	40	13/11	300	300
Vitamin K (µg)	97.3 (63.8-150.0)	98.4 (63.8-139.1)	98.7 (76.4-150.0)	81.0 (75.0-150.0)	120/90	ND	120	120	70	ND	ND
Thiamine (mg)	2.3 (1.5-5.8)	2.3 (1.5-2.5)	2.2 (1.8-3.4)	2.3 (1.8-5.8)	1.2/1.1	ND	1.5	100	0.6	ND	ND
Riboflavin (mg)	2.5 (1.7-7.6)	2.5 (1.7-3.3)	2.7 (2.3-7.6)	2.5 (2.0-3.6)	1.3/1.1	ND	1.2	10	1.6	ND	ND
Niacin (mg)	25.5 (10.2-33.0)	25.5 (10.6-28.9)	21.8 (10.2-30.0)	26.0 (13.0-33.0)	16/14	35	18	40	9.9	ND	ND
Pantothenic acid (mg)	9.0 (6.8-13.3)	8.3 (6.8-13.0)	11.9 (7.6-13.3)	9.0 (7.2-12.8)	5	ND	5	7.5	5	ND	ND
Vitamin B6 (mg)	2.7 (2.0-7.9)	2.6 (2.5-3.8)	2.6 (2.0-7.9)	2.9 (2.5-4.3)	1.3-1.7/1.3-1.5	100	1.5	7.5	1.7/1.6	ND	ND
Biotin (µg)	60.0 (46.9-105.2)	60.0 (46.9-70.1)	91.8 (57.7-105.2)	60.0 (48.0-93.8)	30	ND	30	75	40	ND	ND
Folic acid (µg)	400 (265-1209)	396 (300-447)	324 (266-1209)	414 (300-558)	400	1000	330-400	500	330	1000	1000
Vitamin B12 (µg)	5.4 (3.1-9.6)	4.8 (3.1-6.9)	6.2 (3.5-9.6)	5.9 (3.2-9.4)	2.4	ND	2.5	7.5	4	ND	ND
Vitamin C (mg)	150 (100-1512)	150 (116-180)	278 (100-1512)	156 (105-829)	90/75	2000	100	200	110/95	2000	2000
Sodium (mg)	1246 (510-1589)	1147 (1306-2274)	1471 (605-1589)	1293 (510-1532)	1500	ND	ND	ND	2000	ND	ND
Potassium (mg)	1958 (1306-2700)	1815 (1306-2274)	1990 (1814-2700)	1950 (1442-2419)	3400/2600	ND	ND	ND	3500	ND	ND
Chloride (mg)	1388 (569-2097)	1125 (569-2020)	1677 (630-1803)	1668 (649-2097)	2300	3600	ND	ND	ND	ND	ND
Calcium (mg)	1159 (677-2722)	1088 (677-1820)	1188 (1062-2721)	1200 (764-2025)	1000	2500	ND	ND	1150	2500	2500
Phosphorus (mg)	989 (668-2202)	974 (668-1200)	1061 (956-2202)	987 (679-1200)	700	4000	ND	ND	550	4000	4000
Magnesium (mg)	299 (125-508)	278 (125-345)	332.5 (250-509)	315 (191-345)	420/320	350	ND	ND	350/300	350	350
Iron (mg)	20.0 (11.3-36.3)	20.3 (11.3-24.0)	19.4 (16.0-36.3)	19.7 (15.6-24.0)	8/18	45	18-30	ND	11	45	45
Zinc (mg)	17.6 (12.8-54.4)	17.2 (12.8-19.3)	22.1 (17.5-54.4)	17.5 (14.1-18.4)	11/8	40	10-20	20	9.4-16.3/7.5-12.7	25	25
Copper (µg)	2442 (1500-8226)	2435 (1500-6800)	2564 (2257-8226)	2318 (1500-2700)	900	10000	1000-3000	1000-3000	1600/1300	5000	5000
Iodine (µg)	195 (120-302)	195 (120-240)	219 (188-302)	189 (150-258)	150	1100	150-300	150-300	150	600	600
Selenium (µg)	86.8 (51.0-387.1)	86.0 (67.5-105.0)	79.9 (62.4-387.7)	95.5 (51.0-109.2)	55	400	50-150	200	70	300	300
Chromium (µg)	100.3 (48.8-174.8)	97.6 (48.8-165.0)	139.8 (85.0-157.3)	128.3 (75.0-174.8)	35/25	ND	35-150	200	ND	ND	ND
Molybdenum (µg)	150 (105-238)	150 (113-195)	221 (144-238)	150 (105-177)	45	2000	50-250	250	65	600	600
Manganese (mg)	4.6 (2.0-15.7)	4.8 (2.0-5.6)	3.8 (2.7-15.7)	4.8 (3.0-5.3)	2.3/1.8	11	2-3	2-3	3	11	11

AI: Adequate intake, M: male, f: female, UL: tolerable upper intake levels, DRI: Dietary Reference Intakes, ESPEN: European Society for Clinical Nutrition and Metabolism, TUBER: Türkiye Nutrition Guideline.



**Figure 1.** Proportion of key micronutrient provision by adult enteral formulas relative to recommended daily intake levels according to DRI, ESPEN, and TUBER-2022 Guidelines

The figure illustrates the proportion of key micronutrients supplied by adult enteral formulas available in Türkiye, expressed as a percentage of the recommended daily intake levels based on DRI, ESPEN, and TUBER-2022 guidelines. The red dashed line indicates the 100% adequacy threshold for micronutrient intake.



**Figure 2.** Percentage of micronutrient provision relative to ESPEN high requirement recommendations

The figure illustrates the percentage of recommended intake levels for key micronutrients provided by adult enteral formulas at a 1500 kcal/day intake, specifically evaluated in accordance with ESPEN's high-demand recommendations, which apply to critically ill patients and those with acute malnutrition. The red dashed line represents 100% adequacy.

Discussion

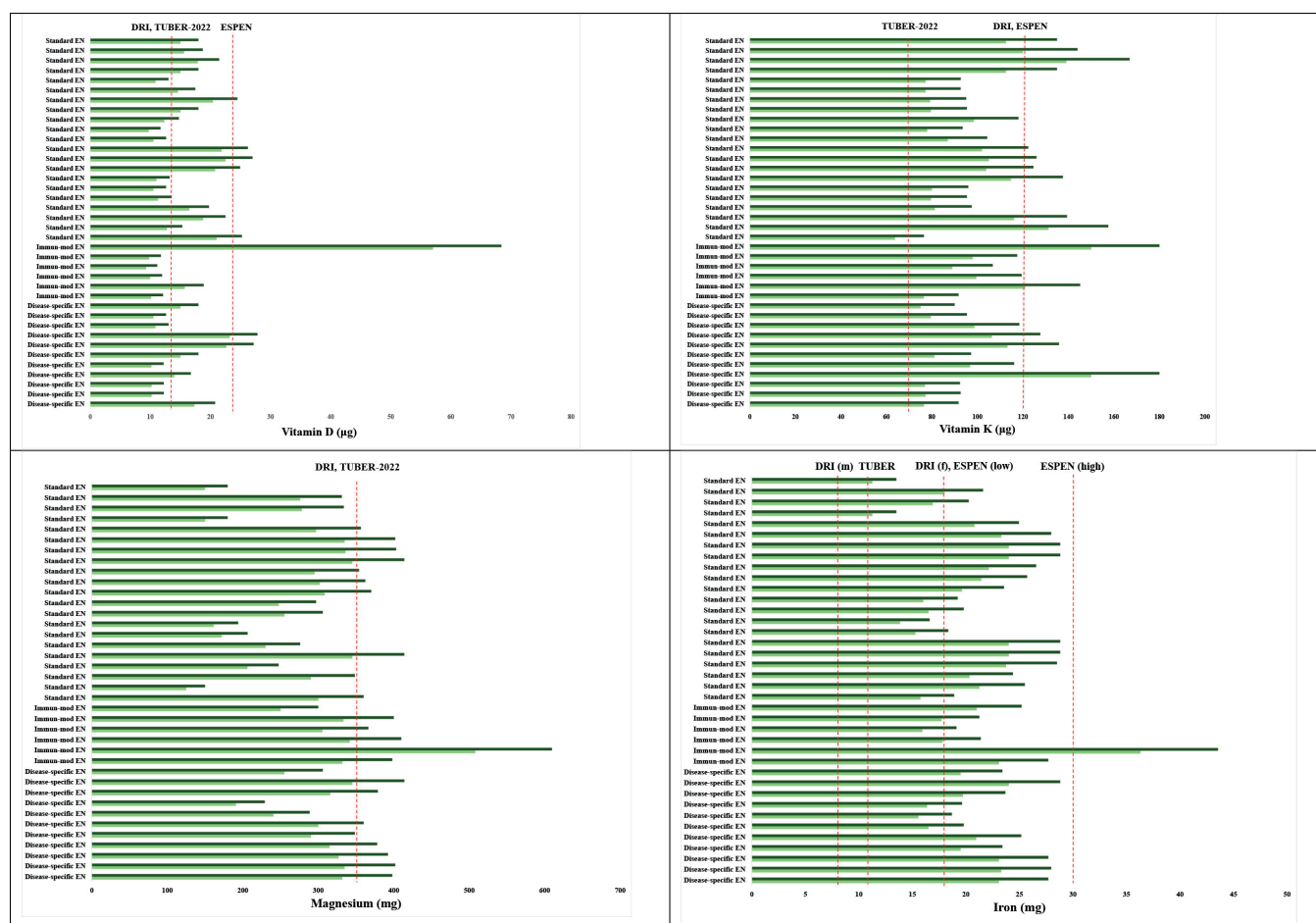
To the best of our knowledge, this is the first study to investigate the micronutrient content of enteral formulas available in Türkiye. The study demonstrated that the intake of vitamin D, vitamin K, magnesium, iron, sodium, potassium, and chloride provided by a 1500 kcal/day enteral formula is insufficient when compared to established reference values. Among these micronutrients, vitamin D, vitamin K, magnesium, and

iron were particularly inadequate in most formulas, as assessed according to the DRI, ESPEN, and TUBER-2022 guidelines, with variations depending on formula type and gender-specific requirements. Additionally, when the higher intake recommendations proposed by ESPEN were considered, inadequacies extended to a broader range of micronutrients, including vitamin A, vitamin E, B-complex vitamins, zinc, selenium, chromium, and molybdenum.

Current guideline emphasize that micronutrient intake is directly influenced by daily energy intake.<sup>5</sup> Existing literature has predominantly focused on the micronutrient intake of hospitalized patients, particularly those in intensive care unit (ICU). A systematic review including nine studies assessing micronutrient intake in ICU patients reported that vitamin B12, vitamin D, vitamin C, vitamin A, thiamine, iron, folate, zinc, and selenium were adequately provided by enteral feeding volumes averaging 826–1600 mL/day, in accordance with the DRIs (7). It is important to note that DRIs typically offer more conservative recommendations tailored to healthy or apparently healthy populations. In contrast, ESPEN guidelines encompass more comprehensive micronutrient recommendations that specifically address the needs of critically ill patients, which may explain discrepancies observed between the two frameworks.

Despite the widespread use of enteral nutrition, studies evaluating micronutrient intake in comparison with ESPEN guidelines remain limited. A study conducted among 81 ICU patients demonstrated that an average enteral nutrition intake of 1037 kcal/day was insufficient





**Figure 3.** The amount of vitamin D, vitamin K, magnesium and iron in enteral formulas

This figure presents the individual contents of micronutrients found to be inadequate—vitamin D, vitamin K, magnesium, and iron—in all evaluated adult enteral formulas available in Türkiye. The red dashed line indicates the 100% adequacy threshold based on recommended intake levels.

to meet ESPEN recommendations for several micronutrients, including vitamins A, D, C, E, as well as selenium, manganese, and zinc.<sup>14</sup> Similarly, a previous study involving 226 ICU patients demonstrated that even when enteral nutrition intake exceeded 1500 kcal/day, the provision of niacin and vitamin D remained insufficient when evaluated in accordance with standard ESPEN guidelines.<sup>15</sup>

Nevertheless, when assessing micronutrient intake, it is crucial to evaluate the actual micronutrient amounts contained in enteral formulas. An evaluation of formula composition reveals that micronutrient inadequacies persist even at commonly recommended energy intakes of 1500–1800 kcal/day. Supporting our findings, Yang et al.<sup>10</sup> investigated the micronutrient content of 31 widely used commercial enteral formulas in China and similarly reported that vitamin D, vitamin K, and iron

intakes at 1500 kcal/day were inadequate according to ESPEN guidelines, despite being sufficient according to the Chinese DRI standards. Likewise, another study evaluating 62 widely used commercial enteral formulas in relation to dietary reference values for European and Italian populations found that at a 1500 kcal/day intake, these formulas provided insufficient amounts of vitamin K and fluoride, while some exceeded the tolerable upper intake levels for zinc and vitamin A.<sup>13</sup> These results collectively indicate that enteral formulas may not consistently ensure adequate micronutrient provision unless caloric intake exceeds specific thresholds. Therefore, the potential need for additional micronutrient supplementation, particularly in patients on long-term enteral nutrition, should be carefully considered.

Patients receiving long-term EN are at increased risk of adverse clinical outcomes due to potential micronutrient

deficiencies.<sup>9</sup> Our findings indicate that EN formulas may inadequately supply vitamin D, vitamin K, magnesium, and iron. Vitamin D, vitamin K, and magnesium are essential for maintaining bone health, muscle function, and immune regulation.<sup>5,16</sup> Deficiencies in these micronutrients have been linked to complications such as impaired immune responses, increased risk of infections, and susceptibility to falls and fractures, although the current study did not assess clinical outcomes at the patient level.<sup>17-19</sup> Additionally, the iron content of the evaluated enteral formulas was notably lower than the reference values, particularly for women of reproductive age. Inadequate iron intake has been associated in the literature with various adverse clinical outcomes, including increased risks of cardiovascular disease, diabetes, certain cancers (such as breast and colorectal cancer), and depression. However, these potential associations were not directly evaluated in this study.<sup>20</sup>

It is particularly important to consider the high-requirement recommendations outlined by ESPEN for critically ill patients and individuals with acute malnutrition. These recommendations are intended for short-term repletion (typically not exceeding 15 days) to avoid the need for intravenous micronutrient supplementation.<sup>5</sup> However, our findings indicate that most of the evaluated enteral formulas fall considerably short of meeting these elevated requirements. This insufficient intake may increase the risk of adverse clinical outcomes, highlighting the importance of careful monitoring, consideration of appropriate supplementation, and possibly reformulation of existing products to better meet clinical needs. Further research assessing patient-level outcomes is warranted.

Furthermore, our data indicated inadequate sodium, potassium, and chloride content in enteral formulas. However, these electrolytes are naturally present in drinking water, and patients receiving enteral nutrition may meet their requirements through additional water intake. Moreover, we did not identify any data indicating adverse clinical outcomes specifically associated with deficiencies of these electrolytes under these conditions.

This study has several limitations that should be acknowledged. First, the micronutrient data were derived from manufacturers' product labels rather than direct laboratory analyses; thus, potential discrepancies between declared and actual nutrient content cannot be ruled out. Second, the analysis was limited to formulas available in the Turkish market, which may limit the generalizability of findings to other countries or regions. Third, only the theoretical nutrient content based on

standardized daily energy intakes (1500 and 1800 kcal/day) was evaluated; actual patient intake may vary due to interruptions in feeding, gastrointestinal tolerance, or clinical conditions. Additionally, this study did not assess the bioavailability or clinical outcomes associated with micronutrient intake, which may further influence nutritional adequacy. Finally, no statistical comparisons or hypothesis testing were performed, as the primary aim of the study was to provide a descriptive evaluation and guideline-based comparison. Additionally, the relatively small sample sizes within each formula subgroup limited the feasibility of meaningful statistical analysis.

In conclusion, this study highlights that adult enteral formulas commonly used in clinical practice may not sufficiently meet the recommended intake levels of several essential micronutrients, particularly when assessed according to ESPEN guidelines. Micronutrient inadequacies, especially in vitamin D, vitamin K, magnesium, and iron, persist even at energy intakes of 1500–1800 kcal/day. These deficiencies may have significant clinical implications, especially for patients on long-term enteral nutrition or those with increased micronutrient requirements, such as critically ill individuals. The potential need for additional micronutrient supplementation should be carefully considered in routine clinical practice to prevent adverse health outcomes. Furthermore, the findings emphasize the importance of revisiting the formulation of enteral products to ensure they adequately address the micronutrient needs of ICU patient populations. Further research is warranted to explore the clinical impact of these inadequacies and to establish optimal supplementation strategies. Specifically, well-designed interventional studies are needed to evaluate the effectiveness and safety of micronutrient supplementation in different patient populations receiving enteral nutrition. Such studies would provide valuable evidence to guide clinical decision-making and improve patient outcomes.

## Ethical approval

Ethical review and approval were waived for this study, as it exclusively analyzed product contents and did not involve experiments with humans or animals.

## Author contribution

The author declare contribution to the paper as follows: Study conception and design: NTÖ; data collection:

NTÖ; analysis and interpretation of results: NTÖ; draft manuscript preparation: NTÖ. The author reviewed the results and approved the final version of the article.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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