Journal of Food Composition and Analysis 123 (2023) 105558

Contents lists available at ScienceDirect

Journal of Food Composition and Analysis

journal homepage: www.elsevier.com/locate/jfca

Vitamin C bioaccessibility of commercially available dietary supplements: Quantity *vs* efficiency, does it matter?

Begüm Hatice Tuna [a], Murat Gürbüz [b], Halime Uğur [c], Jale Çatak [a], Mustafa Yaman [d,e,*]

[a] Department of Nutrition and Dietetics, Faculty of Health Sciences, Istanbul Sabahattin Zaim University, Istanbul, Turkey
[b] Department of Nutrition and Dietetics, Faculty of Health Sciences, Trakya University, Edirne, Turkey
[c] Department of Nutrition and Dietetics, Faculty of Health Sciences, Istanbul Medeniyet University, Istanbul, Turkey
[d] Istanbul Sabahattin Zaim University University Sabri Ülker Food and Nutrition R&D Center, Istanbul, Turkey
[e] Istanbul Sabahattin Zaim University University, Faculty of Engineering and Natural Sciences, Department of Molecular Biology and Genetics, Istanbul, Turkey

ARTICLE INFO

Keywords:
Ascorbic acid
Vitamin C
Bioaccessibility
Dietary supplements
Interaction

ABSTRACT

Knowing the label claims and bioaccessibility of vitamin C supplements is essential for determining daily vitamin C intake. The purpose of the present study was to investigate the bioaccessibility of vitamin C in commercial dietary supplements by an *in vitro* digestion model. In our study, 17 products were examined, including 2 capsules, 15 tablets (9 of these 15 tablet were effervescent tablets). In most commercial dietary supplements, the measured amounts of vitamin C were very close to or higher than the declared amounts. The average measured vitamin C amount of the products were between 90.3 % and 107.5 % of the declared amount. The *in vitro* bioaccessibility of vitamin C in dietary supplements was ranged from 4.0 % to 88.0 %. We observed that the bioaccessibility of vitamin C is higher in mono-supplements compared to multi-supplements. Our results showed that the bioaccessibility of dietary supplements was highly variable. Differences in ingredients of dietary supplements may affect the bioaccessibility of vitamin C. Consequently, the ingredients of the vitamin C supplements and the coating technology used are likely to affect supplementation efficiency.

1. Introduction

Vitamin C, also known as L-ascorbic acid, is one of the essential micronutrients that has important functions in various chemical reactions in cellular metabolism. Humans cannot synthesize vitamin C due to a mutation in the gene encoding L-gulonolactone oxidase, the terminal enzyme in the synthesis pathway of ascorbic acid (Granger and Eck, 2018). Many fruits and vegetables, such as citrus fruits, kiwi, tomatoes, and peppers meet more than 80 % of the daily vitamin C requirement. For this reason, adequate consumption of vegetables and fruits is sufficient to ensure daily vitamin C needs. The European Food Safety Authority (EFSA) recommends a daily vitamin C intake of 110 mg/day and 95 mg/day for men and women over the age of 18, respectively. During pregnancy and lactation, the daily requirement increases due to the transfer of vitamin C to the baby and breast milk. Additionally, heavy smokers (more than 20 cigarettes per day) have an increased daily vitamin C requirement due to severe oxidative stress-induced vitamin C turnover (EFSA, 2013).

In European countries, the daily dietary vitamin C intake of adults ranges from 65 to 139 mg/day (Daud et al., 2016). Vitamin C deficiency can lead to a fatal condition known as scurvy, which is characterized by bleeding gums, pain, and hemorrhage in the extremities (Vissers et al., 2013). In addition, vitamin C deficiency is associated with many diseases such as infections, obesity, cardiovascular diseases, cancer, diabetes, eye diseases, neurodegenerative diseases, psychiatric disorders, bone diseases, skin diseases, and reproductive system diseases (Uğur et al., 2020a). On the other hand, sub-optimal plasma vitamin C levels increase the risk of death of all causes of mortality (Goyal et al., 2013; McKay et al., 2021).

Healthy adults have a total of 300 mg to 2 g of vitamin C in body tissues, with higher concentrations in leukocytes, adrenal glands, brain, and eyes (Daud et al., 2016). Vitamin C is present in many tissues mainly in the form of ascorbic acid (AA) and dehydroascorbic acid (DHAA) (Granger and Eck, 2018). The main function of AA, the bioactive form of vitamin C, in tissues is to reduce free radicals such as reactive oxygen species (ROS). AA loses electrons and is reversibly oxidized to DHAA, thereby reducing oxidative damage in tissues and showing antioxidant activity (Kaur and Nayyar, 2014). The most prominent evidence for

* Corresponding author at: Istanbul Sabahattin Zaim University University Sabri Ülker Food and Nutrition R&D Center, Istanbul, Turkey.
E-mail address: mustafayaman1977@gmail.com (M. Yaman).

https://doi.org/10.1016/j.jfca.2023.105558
Received 11 March 2023; Received in revised form 9 July 2023; Accepted 21 July 2023
Available online 24 July 2023

antioxidant activity comes from the reduction of lipid peroxidation biomarkers and the improvement of DNA damage with vitamin C supplementation (Ferretti et al., 2008; Kawashima et al., 2018; Pasiński et al., 2013). However, it is emphasized that vitamin C supplementation cannot further reduce oxidative damage when the vitamin C in the tissues is at a saturated level (Daud et al., 2016). In understanding this saturation, EFSA assumes that reaching plasma concentrations above about 50 μmol/L significantly increases urinary excretion, reflecting that body pools are near saturation (EFSA, 2013). Vitamin C is also able to regenerate other antioxidant molecules such as glutathione and α-tocopherol by reducing them (Szarka et al., 2012).

Vitamin C plays a cofactor role in many important biochemical reactions such as neurotransmitter synthesis, carnitine synthesis and cross-linking of collagen fibers (Travica et al., 2017). Besides the aforementioned series of biochemical reactions, it is essential for the innate and adaptive immune response. Vitamin C is associated with migration of phagocytes towards infection sites in response to chemoattractants, protection of phagocytic cells and lymphocytes from oxidative stress, natural killer cytotoxic activity, and regulation of the inflammatory response (Carr and Maggini, 2017).

Ascorbic acid supplements can be used in medical treatment to maintain the normal plasma concentration of vitamin C in critically ill patients. In addition to its use in medical treatment, vitamin C supplements also attract the attention of healthy consumers. A multinational Middle Eastern study reported that 47 % of participants used dietary supplements during the second wave of COVID-19 pandemic. Especially vitamin C has been one of the most preferred supplements by consumers (Mukattash et al., 2022). Also, most Americans use dietary supplements to "improve" or "maintain" (45 % and 33 %, respectively) their overall health rather than improve their current diet quality (Dwyer et al., 2022). However, due to COVID-19, vitamin C was one of the dietary supplements with the highest increase (44 %) in use among American adults in the first half of 2020 (Statista, 2020). Commercial companies offer a variety of capsules, tablets, effervescent tablets, and gummy vitamins containing varying doses of vitamin C. However, the main difficulty with ascorbic acid supplements is the high instability characteristic. When ascorbic acid is exposed to heat, transition metal ions, light, and alkaline pH, it is reversibly oxidized to DHAA, and then DHAA is irreversibly hydrolyzed to form 2,3-diketogulonic acid (Uğur et al., 2020a). Therefore, the stability of vitamin C in commercial supplements is essential to maintain supplement quality, label claims, and shelf life. Besides, intestinal factors such as enzymes and alkaline environment significantly affect the stability of vitamin C, causing a decrease in the amount of bioaccessible vitamin C (Rodríguez-Roque et al., 2013; Beceren et al., 2022). Determining the *in vitro* bioaccessibility of vitamin C by mimicking the gastrointestinal tract is the first step towards predicting its biological activity. Basically, *in vitro* bioaccessibility studies offer great advantages due to the absence of ethical problems, low cost, and short-term results (Kamstrup et al., 2017). Also, it is important to calculate the daily nutrient intakes in order to guide individuals properly. Therefore, our study aimed to determine the bioaccessibility of vitamin C in dietary supplements *in vitro* during the three phases of digestion.

2. Materials and methods

L-ascorbic acid (vitamin C), meta-phosphoric acid, pancreatin (8 × USP specifications from pig pancreas), Lipase (Type II from pig pancreas, 100–500 U/mg protein), alpha-amylase (from Aspergillus oryzae powder, 1.5 U/mg), pepsin (from pig gastric mucosa solid, lyophilized powder, 250 U/mg), mucin, NaCl, KCl, $CaCl_2{\cdot}2H_2O$, $NaHCO_3$, urea, bovine serum albumin, uric acid, acetonitrile (ACN), bile salts and other chemicals were obtained from Sigma-Aldrich (St. Louis, MO, USA).

2.1. Sampling

In this study, vitamin C-added dietary supplements were purchased from various pharmacies in Istanbul, Turkey. Of the 17 products analyzed in our study, 2 were capsules, 15 were tablets, and 8 of these 15 tablets were effervescent tablets. The details of these supplements were shown in Table 1.

2.2. In vitro investigation

Bioaccessibility of vitamin C in dietary supplements was determined using the *in vitro* human digestion system. The method described by Uğur et al. (2020b) was used for vitamin C bioaccessibility. Enzymes, organic and inorganic compounds, mouth, stomach, small intestine, and bile solutions were prepared (Fig. 1). In this study, effervescent tablet forms were dissolved with 15 mL of water in 50 mL plastic falcon tubes and then immediately subjected to the *in vitro* digestion. *In* vitro digestion was initiated without pretreatment for tablet and capsule forms.

The digestive system consists of three stages: mouth, stomach, small intestine. In the first step, each dietary supplement (pre-preparation method was indicated above) was mixed with 5 mL of oral medium solution and incubated at 37 °C for 5 min in a shaking water bath. In the second step, the stomach medium was added to the sample obtained after the oral medium and incubated in a shaking water bath at 37 °C for 2 h. In the third step, 10 mL of small intestine medium and 5 mL of bile solution were added into the mix obtained from the stomach phase; the pH was adjusted to 7, and the incubation of the sample was performed for two hours at 37 °C in shaking water bath. After the last digestion was

Table 1
Supplementation form of mono- and multi-vitamin C in the analyzed products.

Product number	Product content	Forms
1	Vitamin C (Orange flavored)	Capsule
2	Vitamin C	Tablet
3	Multi vitamin (Vitamin C, B_1, B_2, B_3, B_5, B_6, B_7, B_9, B_{12}, vitamin A, D, E, K and iron, calcium, zinc, magnesium, copper, iodine, selenium, manganese, molybdenum, coenzyme Q10)	Tablet
4	Vitamin C	Tablet
5	Multi vitamin (Vitamin C, B_1, B_2, B_3, B_5, B_6, B_7, B_9, B_{12}, vitamin A, D, E, K and iron, calcium, zinc, magnesium, copper, iodine, selenium, manganese, molybdenum, beta glucan, probiotic, coenzyme Q10, alpha lipoic acid, lutein)	Capsule
6	Multi vitamin (Vitamin C, B_1, B_2, B_3, B_6, B_9, B_{12}, vitamin E and iron, zinc, selenium, caffeine, green tea extract, ginseng, coenzyme Q10)	Tablet
7	Vitamin C	Effervescent Tablet
8	Vitamin C (Black elderberry flavored)	Effervescent Tablet
9	Vitamin C (Black elderberry flavored)	Effervescent Tablet
10	Vitamin C	Tablet
11	Multi vitamin (Vitamin C, B_1, B_2, B_3, B_5, B_6, B_7, B_9, B_{12}, vitamin A, D, E, K and iron, calcium, zinc, magnesium, copper, iodine, selenium, manganese, molybdenum, phosphorus)	Tablet
12	Vitamin C	Effervescent Tablet
13	Vitamin C (Orange flavored)	Effervescent Tablet
14	Vitamin C (Black elderberry and raspberry flavored)	Effervescent Tablet
15	Vitamin C (Orange flavored)	Effervescent Tablet
16	Vitamin C (Orange flavored)	Effervescent Tablet
17	Vitamin C (Lemon flavored)	Effervescent Tablet

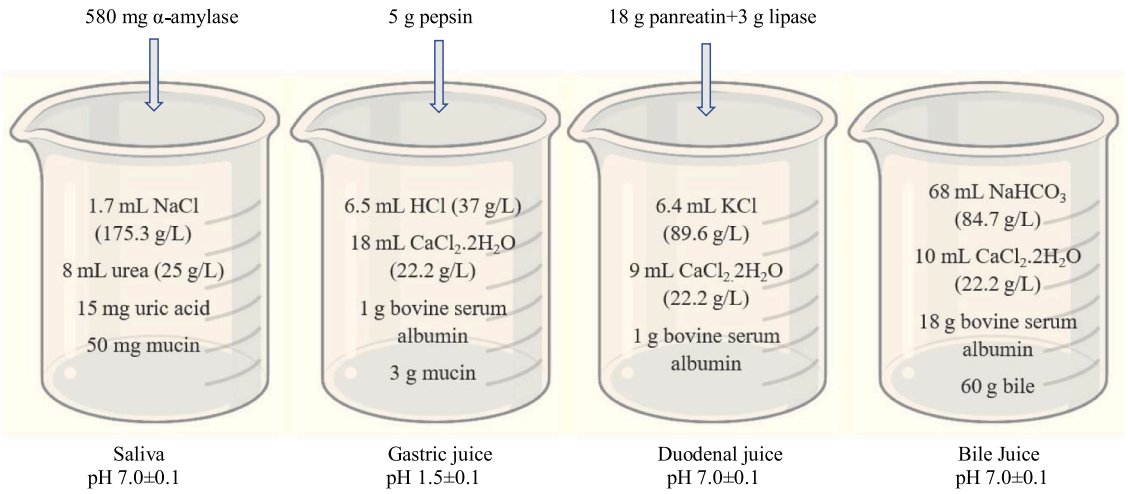

Fig. 1. Components and concentrations of the saliva solution, gastric juice, duodenal juice, and bile juice.

completed, 5 mL of trichloroacetic acid (20 % was added to stop the digestion and then, the final volume of the test sample was made up to 50 mL with deionized water. After that, samples were centrifuged at 8000 rpm for 10 min. Ten mL of each supernatants was mixed with 10 mL of meta-phosphoric acid solution. The solution was then filtered using cellulose acetate (CA) filter (0.45 μm).

2.3. Extraction of vitamin C in dietary supplements

The method described by Uğur et al. (2020b) was applied with some modifications for vitamin C extraction. First, 30 mL of meta-phosphoric acid solution (3 %) was added to dietary supplements (pre-preparation method was indicated above) and vortexed for 5 min. Next, the volume was made up to 50 mL using meta-phosphoric acid solution (3 %). It was then filtered using a CA filter. Finally, the filtrate was moved to HPLC vials before HPLC determination.

2.4. HPLC analysis of vitamin C

Ascorbic acid amounts in the dietary supplements were detected using reverse-phase HPLC. The parameters of HPLC were chosen according to the methodology described by Uğur et al. (2020b). The HPLC system consisted of a Shimadzu LC 20 AT pump by a Shimadzu SPD-20A UV/VIS detector (Shimadzu Corporation, Kyoto, Japan).

Preparation of the mobile phase was accomplished by dissolving 1.24 g of KH_2PO_4 in 1000 mL of deionized water and adjusting to pH 2.4 using ortho-phosphoric acid. Separation was achieved by C18 column (5 μm, 250 ×4.6) (ACE, Scotland). The flow rate was 0.5 mL/min. The wavelength of the detector was 254 nm.

2.5. Statistical analysis

All analyzes were achieved in triplicate, and the mean value was employed. One-way analysis of variance (ANOVA; $p < 0.05$, Tukey's test) was applied to each measure, and significant differences within groups were evaluated statistically.

3. Results and discussion

3.1. Comparison of declared and measured vitamin C amount in dietary supplements

The HPLC chromatogram of L-ascorbic acid in sample 2 is shown in Fig. 2. As seen from the chromatogram, L-ascorbic acid is well separated. Declared and measured vitamin C amounts in dietary supplements are shown in Table 2. Declared vitamin C amounts ranged from 60 to 1000 mg/sample, while measured vitamin C amounts ranged from 50 to 1256 mg/sample. We found that the measured amounts of vitamin C in dietary supplements, overall, ranged from 80 % to 126 % of the declared amount, except for sample 16 (28 %). Previous studies have reported that ascorbic acid was highly unstable, and its amount in food decreases significantly in a short time during storage. Moreover, it has been reported that the loss rate of ascorbic acid is higher as the storage temperature increases (Chávez-Servín et al., 2008; Sahari et al., 2004). In the present study, we found that the average measured amount of vitamin C was 98.06 % of the declared amount in dietary supplements.

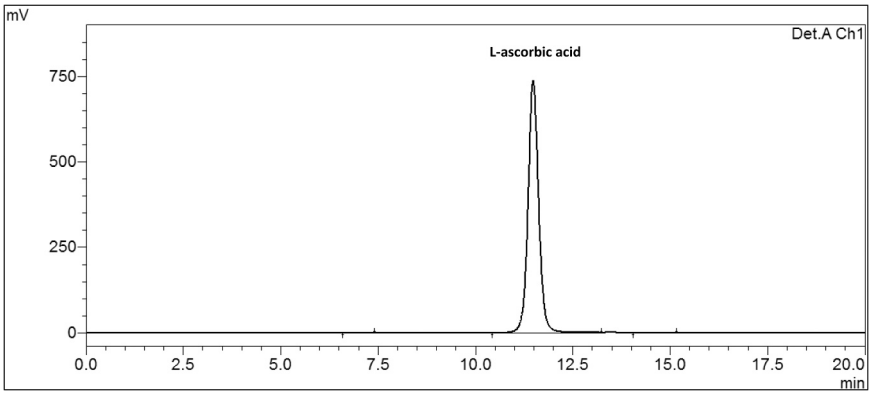

Fig. 2. The HPLC chromatogram of L-ascorbic acid in sample.

Table 2
Comparison of the declared amount of vitamin C (L-ascorbic acid) with the measured amounts in the analyzed products.

Product Number	Declared (mg/100 g)	Measured (mg/100 g)	% of declared
1	500	453 ± 21	91 ± 4
2	500	470 ± 21	94 ± 4
3	80	88 ± 4	110 ± 5
4	150	185 ± 8	124 ± 6
5	120	149 ± 7	124 ± 6
6	100	109 ± 5	109 ± 5
7	1000	1112 ± 50	111 ± 5
8	60	50 ± 2	83 ± 4
9	1000	1047 ± 47	105 ± 5
10	1000	1062 ± 48	106 ± 5
11	100	96 ± 4	96 ± 4
12	1000	1256 ± 57	126 ± 6
13	1000	803 ± 36	80 ± 4
14	100	94 ± 4	94 ± 4
15	1000	903 ± 41	90 ± 4
16	1000	283 ± 13	28 ± 1
17	1000	956 ± 43	96 ± 4

As seen in Table 2, generally, the measured amounts of vitamin C were very close to the declared amount or higher than the declared amounts in most of the products. Similarly, Uğur et al. (2020b) found that the amount of measured vitamin C in baby foods fortified with vitamin C ranged from 135.1 % to 233.1 % of the declared amount. At this point, it is worth noting that overdosing may be a strategy to avoid reaching a concentration below the declared amount of vitamin C due to oxidation during the shelf life of the product. Despite the overdosing strategy, the measured amount in product 16 is considerably lower than the declared amount. This may be due to long shelf life, inappropriate storage conditions, and the application process of the coating technology. Lack of knowledge about the shelf life, storage conditions, and coating technology of these commercial products is an important limitation of the present study.

Of the 17 products analyzed in our study, 2 were capsules, 15 were tablets, and 9 of these 15 tablets were effervescent tablets (Table 1). The average measured vitamin C amount of the products in the form of effervescent tablets, tablets, and capsules were 90.3 %, 106.5 %, and 107.5 % of the declared amount, respectively. The lability of vitamin C can cause a marked decrease in its efficacy. Therefore, the encapsulation of vitamins with increased stability has great potential for applications in the pharmaceutical and food industries. Studies have reported that the encapsulated form of vitamin C shows more stable property with long-term storage, in parallel with our findings (Al-Ismail, 2016; Hassane Hamadou et al., 2020). Besides, the stability of ascorbic acid can also be affected by the presence of other vitamins in the environment. For example, riboflavin has been reported to reduce the stability of ascorbic acid in parenteral solutions (Laborie et al., 1998). In addition, it was emphasized that vitamin C, which is a powerful antioxidant, delays the degradation of vitamin A (Zhou et al., 2021). Actually, the composition and characteristics of commercial multi-supplements vary widely. It is therefore possible for the actual vitamin contents to deviate from the label value. In our study, 4 multi-supplements and 13 mono-supplements containing vitamin C were analyzed. The average amount of vitamin C in multi-supplements was 112 % of that declared, while that of mono-supplements was 93.7 % of that declared. Conversely, Brandon et al. (2014) reported that the amount of vitamin C in mono-supplements was more similar to that declared. This discrepancy may be due to the composition, amount or form of vitamins in multi-supplements.

In commercial dietary supplements, vitamin C is available in the form of free L-ascorbic acid or in combination with sodium and magnesium salts (ascorbic acid derivatives) at the C2 position of ascorbic acid. It also has lipophilic derivatives such as ascorbic acid 6-palmitate and tetra-isopalmitoyl ascorbic acid. Ascorbic acid derivatives generally exhibit better stability than ascorbic acid (Yin et al., 2022). In our study, the form of vitamin C in all dietary supplements was free form of L-ascorbic acid. Vitamin C naturally found in foods mostly exists in the form of coexistence with other dietary compounds and therefore has high stability. For example, it has been reported by Rodriguez-Roque et al. (2013) that antioxidant compounds such as phenols and isoflavones in soy milk increase the stability of ascorbic acid. Han et al. (2012) stated that various ascorbyl glucosides in foods such as berry beverages and black rice baking products have high thermal stability. Additionally, Chanphai and Tajmir-Riahi (2019) reported that vitamin C-protein complexation has more stable properties in an aqueous solution. Therefore, understanding the factors that degrade vitamin C and investigating applications to increase the stability of ascorbic acid are of high importance for designing an effective supplementation strategy.

3.2. *In vitro* bioaccessibility of commercial dietary supplements containing vitamin C

Gastrointestinal system conditions are known to reduce the bioaccessibility of water-soluble vitamins (Yaman and Mızrak Ö, 2019). Yaman et al. (2019) reported that the average bioaccessibility of folic acid in baby foods at gastric pH 1.5 was 58.1 %. Also, Akça et al. (2019) reported that the average bioaccessibility of thiamine, riboflavin, nicotinic acid, and nicotinamide in baby foods were 81 %, 79 %, 39 %, and 51 %, respectively at gastric pH 1.5. However, Uğur et al. (2020b) reported that the bioaccessibility of vitamin C in baby foods at gastric pH 1.5 ranged from 1.3 % to 53.8 %, which was lower than that of B group vitamins. Similar to previous findings, our results also showed that the bioaccessibility of vitamin C was decreased as a result of digestion. In the present study, the bioaccessibility of vitamin C in dietary supplements was determined through an *in vitro* digestion model representing the mouth, stomach, and small intestine. The bioaccessible amount and percent bioaccessibility of vitamin C are shown in Table 3.

Consumption of 5 servings of vegetables and fruits, as recommended by global health authorities for adults, can provide adequate daily dietary vitamin C intake (Taylor et al., 2000). However, dietary vitamin C intake may not be sufficient in critically ill patients due to the increase in daily requirements (Mahmoodpoor et al., 2021). Vitamin C can be easily oxidized by contact with gastrointestinal system-specific factors such as enzymes, heat and alkaline environment (Rodríguez-Roque et al., 2013). Therefore, supplementation is necessary when the level of vitamin C in the tissues is depleted (Xing et al., 2021). Determining the bioaccessibility of vitamin C is requisite as well as shelf life for effective

Table 3
In vitro bioaccessibility of vitamin C (L-ascorbic acid) in analyzed products.

Product number	Initial value (mg)	After *in vitro* digestion (mg)	Bioaccessibility (%)
1	453 ± 21^{a}	399 ± 14^{b}	88 ± 7
2	470 ± 21^{a}	406 ± 14^{b}	86 ± 7
3	88 ± 4^{a}	4 ± 0^{b}	4 ± 0
4	185 ± 8^{a}	105 ± 4^{b}	57 ± 5
5	149 ± 7^{a}	26 ± 1^{b}	17 ± 1
6	109 ± 5^{a}	$51 \pm {}^{2b}$	47 ± 4
7	1112 ± 50^{a}	672 ± 24^{b}	61 ± 5
8	50 ± 2^{a}	23 ± 1^{b}	46 ± 4
9	1047 ± 47^{a}	734 ± 26^{b}	70 ± 6
10	1062 ± 48^{a}	840 ± 30^{b}	79 ± 6
11	96 ± 4^{a}	17 ± 1^{b}	18 ± 1
12	1256 ± 57^{a}	960 ± 34^{b}	77 ± 6
13	803 ± 36^{a}	608 ± 21^{b}	76 ± 6
14	94 ± 4^{a}	78 ± 3^{b}	83 ± 7
15	903 ± 41^{a}	720 ± 25^{b}	80 ± 6
16	283 ± 13^{a}	203 ± 7^{b}	72 ± 6
17	956 ± 43^{a}	773 ± 27^{b}	81 ± 7

Values are means ± range, n = 3. The different letters in the same rows show statistical differences between the initial value and after *in vitro* digestions (ANOVA, $p < 0.05$, Tukey's test).

supplementation strategies in commercial supplements. Brandon et al. (2014) has been reported that the bioaccessibility of vitamin C in dietary supplements ranged from 1.0 % to 100 %. Similarly, we found that the bioaccessibility of vitamin C in commercial dietary supplements ranged from 4.0 % to 88.0 %. The main challenge in the bioavailability of vitamin C is to increase the bioaccessible amount by maintaining controlled release and stability in the gastrointestinal tract. To date, various strategies such as tablet coating and encapsulation have been developed to provide an adequate delivery system for nutrients sensitive to gastrointestinal tract conditions. Hu et al. (2020) designed a new salecan/chitosan polyelectrolyte complex hydrogel targeting the controlled release of vitamin C in the gastrointestinal tract. Similarly, it has been reported that the controlled release of vitamin C encapsulated in casein gel was improved in simulated gastric and intestinal fluid (Yan et al., 2021). In addition to gelatin, capsules containing polymers such as hydroxyl propyl methylcellulose are produced to achieve controlled release in the gastrointestinal tract (Marzorati et al., 2021). In our study, the *in vitro* bioaccessibility of dietary supplements with tablet, capsule, and effervescent tablet form ranged from 4 % to 86 %, 46–83 %, and 17–88 %, respectively. One of the reason why the bioaccessibility of dietary supplements is widely variable may be due to the different characteristics of the tablet coating and encapsulation technology and materials used. In addition, factors specific to the gastrointestinal system such as enzymes, heat, alkalinity, as well as some B group vitamins (B_1, B_2, and B_{12}), metal ions, vitamin-binding proteins, and multiple supplements used may change the bioaccessibility of vitamin C (Yaman et al., 2021). Brandon et al. (2014) reported that the bioaccessibility of vitamin C was lower in the fed condition than in the fasted condition, indicating that some of the vitamin C was lost during digestion with other nutrients. On the contrary, Beceren et al. (2022) suggested that milk proteins that are resistant to digestion may increase the bioaccessibility of vitamin C. Further, it is reported that soy milk phenols and isoflavones increase the bioaccessibility of vitamin C because of their antioxidant activity (Rodríguez-Roque et al., 2015). However, the presence of metal ions such as Cu^{2+} and Fe^{2+} may reduce the bioaccessibility of vitamin C by causing its decomposition (Dosedël et al., 2021). These factors will cause differences in the release of vitamin C from products containing the same amount of vitamin C, thereby affecting bioaccessibility and thus supplement effectiveness.

In the early 20th century, vitamins in foods were isolated, purified, and produced as dietary supplements (El Ati-Hellal and Hellal, 2021). These vitamins are now commercially produced as mono- and multi-supplements and placed on the market for consumer use. Especially during the pandemic period, the use of vitamin supplements by consumers has increased significantly. Interestingly, vitamin C has been one of the most preferred supplements by consumers (Hamulka et al., 2020). According to the National Health and Nutrition Examination Survey (NHANES) 2011–2014 data, multivitamin supplements account for the vast majority of total dietary supplement use (Cowan et al., 2018). Turkey Nutrition and Health Survey (TNHS) reported that multivitamin supplements accounted for approximately 14 % of total dietary supplement use in the Turkish adult population in 2017. However, the effect of amount and composition differences in vitamin supplements on bioaccessibility has not been clearly clarified until now. Brandon et al. (2014) reported that the bioaccessibility of vitamin C is higher in mono-supplements compared to multi-supplements. The authors suggested that the different bioaccessibility values were due to differences in encapsulation of vitamin C between mono- and multi-vitamin supplements. Similarly, we observed the average bioaccessibility of vitamin C in multi- and mono-supplements as 21.5 % and 73.5 %, respectively. We also observed that the low bioaccessibility of multi-supplements is independent of the capsule or tablet form of the commercial dietary supplement.

The health effect value of vitamins in foods and food supplements is difficult to predict due to their poorly known bioaccessibility. Therefore, it is essential to clearly elucidate the micronutrients, vitamin binders, and gastrointestinal tract factors that affect the bioaccessibility of vitamin C (Yaman et al., 2021). Actually, a balanced diet allows most of nutrients to interact with vitamin C in the gastrointestinal tract. However, limited evidence has noted that the bioaccessibility of vitamin C is not adversely affected by other food sources (Brandon et al., 2014; Cilla et al., 2012). Overall, literature data has suggested that the bioaccessibility of vitamin C in dietary supplements is affected by the nutrient composition of the commercial product and the capsule technology used, rather than the nutritional status.

4. Conclusions

The vitamin supplements market attracts the consumers due to various claims on overall human wellness. Especially vitamin C has been one of the most popular supplements by consumers during the COVID-19 pandemic. Consumption of 5 servings of vegetables and fruits can provide adequate daily dietary vitamin C. However, supplementation can be necessary when the level of vitamin C in the tissues is depleted. Vitamin C is a highly unstable molecule, and its amount can decrease significantly in a short time during storage. However, we found the amount of vitamin C in dietary supplements close to or higher than the declared amount. This may be due to overdosing and this may be a good strategy for manufacturers to avoid reaching a concentration below the declared amount of vitamin C and to validate their label claims during the shelf life. Also, the encapsulated form of vitamin C had the most stable characteristic and therefore the encapsulation of vitamins with increased stability has great potential for pharmaceutical and food industries.

Vitamin C can be easily oxidized by contact with factors specific to the gastrointestinal tract such as enzymes, heat, and an alkaline environment. As well as label claims and shelf life, determining the bioaccessibility of vitamin C is also crucial to effective supplementation strategies for both consumers and manufacturers. We found that the bioaccessibility of vitamin C in commercial dietary supplements was highly variable, ranging from 4.0 % to 88.0 %. The reasons why the bioaccessibility of dietary supplements is widely variable may be due to the different characteristics of the tablet coating and encapsulation technology and materials used. Additionally, we observed that the bioaccessibility of vitamin C was higher in mono-supplements compared to multi-supplements and the low bioaccessibility of multi-supplements was independent of the capsule or tablet form of the commercial dietary supplement. Some proteins, vitamins, and metal ions may affect the bioaccessibility of vitamin C in multiple supplements. However, data on ingredients such as vitamins, minerals, and non-nutrient compounds that may affect the bioaccessibility of vitamin C in multi-supplements need to be clarified by further studies.

In conclusion, we inferred that the bioaccessibility of vitamin C in dietary supplements can be significantly affected by the nutrient composition and the production technology of commercial products. Therefore, both producers and consumers should focus on efficiency rather than quantity for more effective supplement strategies.

CRediT authorship contribution statement

Begüm Hatice Tuna: Formal analysis, Investigation. **Murat Gürbüz:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Halime Uğur:** Methodology, Writing – original draft, Writing – review & editing. **Jale Çatak:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Mustafa Yaman:** Investigation, Methodology, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

Data availability

No data was used for the research described in the article.

References

Akça, S.N., Sargın, H.S., Mızrak, Ö.F., Yaman, M., 2019. Determination and assessment of the bioaccessibility of vitamins B1, B2, and B3 in commercially available cereal-based baby foods. Microchem. J. 150, 104192 https://doi.org/10.1016/j.microc.2019.104192.

Al-Ismail, K., 2016. Effect of microencapsulation of vitamin C with gum arabic, whey protein isolate and some blends on its stability. J. Sci. Ind. Res. 75, 176–180.

Beceren, Y., Gürbüz, M., Çatak, J., Demir, B., Uğur, H., Yaman, M., 2022. In vitro bioaccessibilities of vitamin C in baby biscuits prepared with or without UHT cow's milk. J. Food Compos. Anal., 104706 https://doi.org/10.1016/j.jfca.2022.104706.

Brandon, E.F., Bakker, M.I., Kramer, E., Bouwmeester, H., Zuidema, T., Alewijn, M., 2014. Bioaccessibility of vitamin A, vitamin C and folic acid from dietary supplements, fortified food and infant formula. Int J. Food Sci. Nutr. 65 (4), 426–435. https://doi.org/10.3109/09637486.2013.869795.

Carr, A.C., Maggini, S., 2017. Vitamin C and immune function. Nutrients 9 (11), 1211. https://doi.org/10.3390/nu9111211.

Chanphai, P., Tajmir-Riahi, H.A., 2019. Conjugation of vitamin C with serum proteins: a potential application for vitamin delivery. Int J. Biol. Macromol. 137, 966–972. https://doi.org/10.1016/j.ijbiomac.2019.07.059.

Chávez-Servín, J., Castellote, A., Rivero, M., López-Sabater, M., 2008. Analysis of vitamins A, E and C, iron and selenium contents in infant milk-based powdered formula during full shelf-life. Food Chem. 107, 1187–1197. https://doi.org/10.1016/j.foodchem.2007.09.048.

Cilla, A., Alegría, A., de Ancos, B., Sánchez-Moreno, C., Cano, M.P., Plaza, L., Barberá, R.. (2012). Bioaccessibility of tocopherols, carotenoids, and ascorbic acid from milk- and soy-based fruit beverages: influence of food matrix and processing. J. Agric. Food Chem., 60(29), 7282–7290. https://doi.org/10.1021/jf301165r.

Cowan, A.E., Jun, S., Gahche, J.J., Tooze, J.A., Dwyer, J.T., Eicher-Miller, H.A., Bailey, R.L., 2018. Dietary supplement use differs by socioeconomic and health-related characteristics among U.S. adults, NHANES 2011¯2014. *Nutrients* 10 (8). https://doi.org/10.3390/nu10081114.

Daud, Z., Ismail, A., Sarmadi, B., 2016. Ascorbic acid: physiology and health effects. Encycl. Food Health. https://doi.org/10.1016/B978-0-12-384947-2.00045-3.

Doseděl, M., Jirkovský, E., Macáková, K., Krčmová, L.K., Javorská, L., Pourová, J., On Behalf Of The, O, 2021. Vitamin C-sources, physiological role, kinetics, deficiency, use, toxicity, and determination. Nutrients 13 (2), 615. https://doi.org/10.3390/nu13020615.

Dwyer, J.T., Saldanha, L.G., Bailen, R., 2022. Dietary supplement databases: public health tools. J. Food Compos. Anal. 105, 104244.

EFSA, 2013. Scientific opinion on dietary reference values for vitamin C. EFSA J. 11 (11), 3418.

El Ati-Hellal, M., Hellal, F., 2021. Food Supplementation with Vitamins and Minerals: An Overview. https://doi.org/10.5772/intechopen.98287.

Ferretti, G., Bacchetti, T., Masciangelo, S., Pallotta, G., 2008. Lipid peroxidation in hemodialysis patients: effect of vitamin C supplementation. Clin. Biochem. 41 (6), 381–386. https://doi.org/10.1016/j.clinbiochem.2007.12.011.

Goyal, A., Terry, M.B., Siegel, A.B., 2013. Serum antioxidant nutrients, vitamin A, and mortality in U.S. Adults. Cancer Epidemiol. Biomark. Prev. 22 (12), 2202–2211. https://doi.org/10.1158/1055-9965.Epi-13-0381.

Granger, M., Eck, P., 2018. Chapter Seven - Dietary Vitamin C in Human Health. In: Eskin, N.A.M. (Ed.), Advances in Food and Nutrition Research, Vol. 83. Academic Press, pp. 281–310. https://doi.org/10.1016/bs.afnr.2017.11.006.

Hamulka, J., Jeruszka-Bielak, M., Górnicka, M., Drywień, M., Zielińska-Pukos, M., 2020. Dietary supplements during COVID-19 outbreak. Results of Google trends analysis supported by PLifeCOVID-19 online studies. Nutrients 13, 54. https://doi.org/10.3390/nu13010054.

Han, R., Liu, L., Li, J., Du, G., Chen, J., 2012. Functions, applications and production of 2-O-D-glucopyranosyl-L-ascorbic acid. Appl. Microbiol Biotechnol. 95 (2), 313–320. https://doi.org/10.1007/s00253-012-4150-9.

Hassane Hamadou, A., Huang, W.-C., Xue, C., Mao, X., 2020. Formulation of vitamin C encapsulation in marine phospholipids nanoliposomes: characterization and stability evaluation during long term storage. LWT 127, 109439. https://doi.org/10.1016/j.lwt.2020.109439.

Hu, X., Wang, Y., Zhang, L., Xu, M., 2020. Formation of self-assembled polyelectrolyte complex hydrogel derived from salecan and chitosan for sustained release of Vitamin C. Carbohydr. Polym. 234, 115920 https://doi.org/10.1016/j.carbpol.2020.115920.

Kamstrup, D., Berthelsen, R., Sassene, P.J., Selen, A., Müllertz, A., 2017. In vitro model simulating gastro-intestinal digestion in the pediatric population (Neonates and Young Infants). AAPS PharmSciTech 18 (2), 317–329. https://doi.org/10.1208/s12249-016-0649-1.

Kaur, R., Nayyar, H., 2014. Chapter 8 - Ascorbic acid: a potent defender against environmental stresses. In: Ahmad, P. (Ed.), Oxidative Damage to Plants. Academic Press, pp. 235–287. https://doi.org/10.1016/B978-0-12-799963-0.00008-3.

Kawashima, S., Funakoshi, T., Sato, Y., Saito, N., Ohsawa, H., Kurita, K., Ishigami, A. (2018). Protective effect of pre- and post-vitamin C treatments on UVB-irradiation-induced skin damage. Sci. Rep, 8(1), 16199. https://doi.org/10.1038/s41598-018-34530-4.

Laborie, S., Lavoie, J.C., Chessex, P., 1998. Paradoxical role of ascorbic acid and riboflavin in solutions of total parenteral nutrition: implication in photoinduced peroxide generation. Pediatr. Res. 43 (5), 601–606. https://doi.org/10.1203/00006450-199805000-00007.

Mahmoodpoor, A., Shadvar, K., Sanaie, S., Hadipoor, M.R., Pourmoghaddam, M.A., Saghaleini, S.H., 2021. Effect of Vitamin C on mortality of critically ill patients with severe pneumonia in intensive care unit: a preliminary study. BMC Infect. Dis. 21 (1), 616. https://doi.org/10.1186/s12879-021-06288-0.

Marzorati, M., Calatayud, M., Rotsaert, C., Van Mele, M., Duysburgh, C., Durkee, S., Bellamine, A., 2021. Comparison of protection and release behavior of different capsule polymer combinations based on L. acidophilus survivability and function and caffeine release. Int. J. Pharm. 607, 120977 https://doi.org/10.1016/j.ijpharm.2021.120977.

McKay, G.J., Lyner, N., Linden, G.J., Kee, F., Moitry, M., Biasch, K.,. Woodside, J.V. (2021). Association of low plasma antioxidant levels with all-cause mortality and coronary events in healthy middle-aged men from France and Northern Ireland in the PRIME study. Eur. J. Nutr, 60(5), 2631–2641. https://doi.org/10.1007/s00394-020-02455-2.

Mukattash, T.L., Alkhalidy, H., Alzu'bi, B., Abu-Farha, R., Itani, R., Karout, S., Jarab, A. (2022). Dietary supplements intake during the second wave of COVID-19 pandemic: a multinational Middle Eastern study. Eur. J. Integr. Med., 49, 102102–102102. https://doi.org/10.1016/j.eujim.2022.102102.

Pasiński, J., Swierczewski, A., Estemberg, D., Kowalska-Koprek, U., Karowicz-Bilińska, A. (2013). [The influence of vitamin C and E use on concentration of endothelin-1 and lipid peroxides in the serum of pregnant women with arterial hypertension]. Ginekol. Pol., 84(1), 32–37. https://doi.org/10.17772/gp/1537 (Wplyw przyjmowania witaminy C oraz E na stezenie endoteliny-1 oraz nadtlenków lipidów w surowicy kobiet ciezarnych z nadciśnieniem tetniczym.).

Republic of Turkey Ministry of Health General Director of Public Health. Turkey Nutrition and Health Survey 2017 (TNHS 2017); Tiraj Basım ve Yayın Sanayi Ticaret Ltd. Sti.: Ankara, Turkey, 2019; ISBN 978–975-590–722-2.

Rodríguez-Roque, M.J., Rojas-Graü, M.A., Elez-Martínez, P., Martín-Belloso, O., 2013. Changes in vitamin C, phenolic, and carotenoid profiles throughout in vitro gastrointestinal digestion of a blended fruit juice. J. Agric. Food Chem. 61 (8), 1859–1867. https://doi.org/10.1021/jf3044204.

Rodríguez-Roque, M.J., de Ancos, B., Sánchez-Moreno, C., Pilar Cano, M., Elez-Martínez, P., Martín-Belloso, O., 2015. Impact of food matrix and processing on the in vitro bioaccessibility of vitamin C, phenolic compounds, and hydrophilic antioxidant activity from fruit juice-based beverages. J. Funct. Foods 14 (*2015*), *33–43*.

Sahari, M.A., Mohsen Boostani, F., Zohreh Hamidi, E., 2004. Effect of low temperature on the ascorbic acid content and quality characteristics of frozen strawberry. Food Chem. 86 (3), 357–363. https://doi.org/10.1016/j.foodchem.2003.09.008.

Statista. (2020). Dietary supplements with largest increase in usage due to COVID-19 among U.S. adults as of August 2020. https://www.statista.com/statistics/1180337/top-dietary-supplement-usage-growth-due-to-covid-us-adults/.

Szarka, A., Tomasskovics, B., Bánhegyi, G., 2012. The ascorbate-glutathione-α-tocopherol triad in abiotic stress response. Int. J. Mol. Sci. 13 (4), 4458–4483. https://doi.org/10.3390/ijms13044458.

Taylor, C., Hampl, J., Johnston, C., 2000. Low intakes of vegetables and fruits, especially citrus fruits, lead to inadequate vitamin C intakes among adults. Eur. J. Clin. Nutr. 54, 573–578. https://doi.org/10.1038/sj.ejcn.1601059.

Travica, N., Ried, K., Sali, A., Scholey, A., Hudson, I., Pipingas, A., 2017. Vitamin C status and cognitive function: a systematic review. Nutrients 9 (9), 960. https://doi.org/10.3390/nu9090960.

Uğur, H., Eker, S., Çatak, J., Yaman, M., 2020a. Vitamin C ve hastalıklar üzerine etkisi. Avrupa Bilim ve Teknol. Derg. 19, 746–756.

Uğur, H., Çatak, J., Mızrak, Ö., F., Çebi, N., Yaman, M., 2020b. Determination and evaluation of in vitro bioaccessibility of added vitamin C in commercially available fruit-, vegetable-, and cereal-based baby foods. Food Chem. 330, 127166 https://doi.org/10.1016/j.foodchem.2020.127166.

Vissers, M.C., Carr, A.C., Pullar, J.M., Bozonet, S.M., 2013. The bioavailability of vitamin C from kiwifruit. Adv. Food Nutr. Res 68, 125–147. https://doi.org/10.1016/b978-0-12-394294-4.00007-9.

Xing, Y., Zhao, B., Yin, L., Guo, M., Shi, H., Zhu, Z., Zhang, L., 2021. Vitamin C supplementation is necessary for patients with coronavirus disease: an ultra-high-performance liquid chromatography-tandem mass spectrometry finding. J. Pharm. Biomed. Anal. 196, 113927 https://doi.org/10.1016/j.jpba.2021.113927.

Yaman M., Mızrak Ö. F. (2019). Determination and evaluation of in vitro bioaccessibility of the pyridoxal, pyridoxine, and pyridoxamine forms of vitamin B(6) in cereal-based baby foods. Food Chem., 298, 125042. https://doi.org/10.1016/j.foodchem.2019.125042.

Yaman, M., Mızrak, Ö., F., Çatak, J., Sargın, H.S., 2019. In vitro bioaccessibility of added folic acid in commercially available baby foods formulated with milk and milk products. Food Sci. Biotechnol. 28 (6), 1837–1844. https://doi.org/10.1007/s10068-019-00625-5.

Yaman, M., Çatak, J., Uğur, H., Gürbüz, M., Belli, İ., Tanyıldız, S.N., Yaldız, M.C., 2021. The bioaccessibility of water-soluble vitamins: a review. Trends Food Sci. Technol. 109, 552–563. https://doi.org/10.1016/j.tifs.2021.01.056.

Yan, B., Davachi, S.M., Ravanfar, R., Dadmohammadi, Y., Deisenroth, T.W., Pho, T.V., Abbaspourrad, A., 2021. Improvement of vitamin C stability in vitamin gummies by

encapsulation in casein gel. Food Hydrocoll. 113, 106414 https://doi.org/10.1016/j.foodhyd.2020.106414.
Yin, X., Chen, K., Cheng, H., Chen, X., Feng, S., Song, Y., Liang, L., 2022. Chemical stability of ascorbic acid integrated into commercial products: a review on bioactivity and delivery technology. Antioxidants (Basel) 11 (1). https://doi.org/10.3390/antiox11010153.
Zhou, H.B., Huang, X.Y., Bi, Z., Hu, Y.H., Wang, F.Q., Wang, X.X., Lu, Z.Q., 2021. Vitamin A with L-ascorbic acid sodium salt improves the growth performance, immune function and antioxidant capacity of weaned pigs. Animal 15 (2), 100133. https://doi.org/10.1016/j.animal.2020.100133.