Hindawi
Journal of Nutrition and Metabolism
Volume 2020, Article ID 5349086, 7 pages
https://doi.org/10.1155/2020/5349086

Research Article

Miso Soup Consumption Enhances the Bioavailability of the Reduced Form of Supplemental Coenzyme Q_{10}

Michiyo Takahashi,[1] Mayumi Nagata,[2] Takehiko Kaneko,[1,2] and Toshikazu Suzuki [1,2]

[1]*Graduate School of Human Ecology, Wayo Women's University, 2-3-1 Konodai, Ichikawa, Chiba 272-8533, Japan*
[2]*Department of Health and Nutrition, Wayo Women's University, 2-3-1 Konodai, Ichikawa, Chiba 272-8533, Japan*

Correspondence should be addressed to Toshikazu Suzuki; t-suzuki@wayo.ac.jp

Received 31 August 2019; Accepted 25 November 2019; Published 7 January 2020

Academic Editor: C. S. Johnston

Coenzyme Q_{10} (CoQ_{10}) is an essential compound that is involved in energy production and is a lipid-soluble antioxidant. Although it has been proposed as an antiaging and a health-supporting supplement, its low bioavailability remains a significant issue. Concurrent food intake enhances the absorption of orally administered CoQ_{10}, but it has not been fully established whether specific food substances affect intestinal CoQ_{10} absorption. Therefore, to determine whether the bioavailability of supplemental CoQ_{10} is affected by diet, P30, a granulated and reduced form of CoQ_{10}, was dispersed in four different foods, clear soup, miso soup, milk soup, and raw egg sauce. Those foods which contained CoQ_{10} were consumed on different occasions at intervals of 6–14 weeks by the same participants. Thirteen participants were recruited in the single-dose and repeated clinical study. When miso soup containing P30 was provided, the serum CoQ_{10} concentration increased faster than when participants consumed other P30-containing soups or a P30-containing raw egg sauce. The area under the curve for serum CoQ_{10} during the first 5 h after consumption of the P30-containing miso soup was approximately 1.5 times larger than those after the consumption of other P30-containing meals. These data imply that the absorption of CoQ_{10} supplements can be enhanced by consuming them with food and in particular with specific food substances, such as miso soup.

1. Introduction

Coenzyme Q_{10} (CoQ_{10}), a vitamin-like substance, is involved in energy production and is a lipid-soluble antioxidant [1–3]. Many studies have reported a relationship between CoQ_{10} and aging. For example, the amount of CoQ_{10} in muscles and organs decreases with age [4], as does the serum CoQ_{10} concentration and that of the reduced form [5] in healthy adults. Both blood levels and the ratio of the reduced form of CoQ_{10} concentration to total coenzyme Q_{10} in hospitalized elderly people were lower than that in the healthy elderly people [6]. Also, many studies have shown associations between serum CoQ_{10} status and health [7–11]. In addition, CoQ_{10} supplementation has been shown to ameliorate the symptoms of some geriatric disorders and to improve the quality of life of humans and some laboratory animals. CoQ_{10} supplementation ameliorates high blood pressure [12], glucose metabolism in diabetes [13], and the symptoms of Parkinson's disease [14] and reduces peripheral oxidative stress and inflammation in interferon β-1a-treated multiple sclerosis [15]. It can also increase the vitality of patients undergoing medical treatment and of the elderly residents of nursing homes [16–18]. Furthermore, it alleviates fatigue in patients with chronic fatigue syndrome [19, 20], hyperlipidemia [21], and in those with end-stage heart failure awaiting cardiac transplantation [22]. In older rats, CoQ_{10} supplementation has been shown to alleviate diabetes-induced learning and memory deficits and to improve cognitive performance when administered at a high dose [23]. In the senescence-accelerated prone 8 mouse, CoQ_{10} supplementation counteracts the deleterious effects of physical exercise-derived reactive oxygen species, improving mitochondrial function [24]. Thus, CoQ_{10} may be useful as an antiaging and health-supporting supplement.

In general, the absorption of compounds from the gastrointestinal tract is one of the most important determinants of oral bioavailability. Intestinal absorption of supplemental CoQ_{10} is slow and limited because of the compound's hydrophobicity and high molecular weight. Many types of CoQ_{10} delivery system have been developed that aim to increase the bioavailability of supplemental CoQ_{10}, such as self-emulsifying drug delivery systems, nanotechnology-based drug delivery systems, cyclodextrin complexes, CoQ_{10}-solanesyl poly(ethylene glycol) succinate micelles, and a reduced form of CoQ_{10} that is both emulsified and solubilized [25–27]. In addition, the concurrent consumption of food enhances the rate of the absorption of orally administered supplemental CoQ_{10} [28]. Therefore, the consumption of CoQ_{10}-fortified foods may be a useful way of increasing the bioavailability of CoQ_{10}.

It is well known that the absorption of nutrients, such as vitamins and minerals, is affected by the food items concurrently consumed or their components. For example, the enhancement of β-carotene absorption by mayonnaise consumption [29], of carotenoid absorption by avocado or avocado oil consumption [30], of vitamin E absorption by egg consumption [31], and of nonheme iron absorption by meat protein and vitamin C consumption, have been reported [32–34]. Conversely, some dietary fibers suppress the absorption of β-carotene, lycopene, and lutein [35]. Additionally, tannins, phytic acid, polyphenols, and calcium inhibit the absorption of nonheme iron [36–39]. Thus, the absorption of supplemental CoQ_{10} may also be affected by the food or a component with which it is consumed, although no previous studies have addressed this issue. Therefore, knowledge of the food items that could enhance the absorption of orally administered CoQ_{10} is crucial for the development of appropriate functional CoQ_{10}-fortified foods.

Previously, we investigated the association between dietary habits and serum CoQ_{10} levels before and after long-term supplementation with a reduced form of CoQ_{10} [40, 41]. People with higher basal serum CoQ_{10} concentrations tended to consume more soy products [40], and those who had a higher increase in serum CoQ_{10} concentrations after the 1-year supplementation tended to consume more dairy products and eggs [41]. These results remind us that soy products, dairy products, and eggs might positively affect the absorption of CoQ_{10} supplements.

In this study, we investigated the effect of various foods on the bioavailability of supplemental CoQ_{10} using P30, a granulated and reduced form of CoQ_{10} supplement, and a typical Japanese meal, consisting of steamed rice, grilled salmon with marinated Japanese radish, boiled spinach, and soup. P30 was suspended in the soup or raw egg sauce in advance, before being provided to the participants. Miso soup, milk soup, and raw egg sauce were used as foods containing soy products, daily products, and eggs, respectively. Clear soup, which is seasoned with salt, was used as a reference food. The soup consumed was different in each experiment. Serum CoQ_{10} concentration was determined before, and 1.5, 3, and 5 h after eating the meals, and the bioavailability of CoQ_{10} was compared among the various foods that were concurrently consumed.

2. Materials and Methods

2.1. CoQ_{10} Supplements. A granulated, solubilized, and reduced form of CoQ_{10} supplement, P30, was used in the study. P30 contains 30 w/w% of reduced CoQ_{10} (120 mg per sachet), dextrin, gum Arabic, and L-ascorbate. These supplements were provided by the Kaneka Corporation (Osaka, Japan).

2.2. Study Design. Thirteen healthy volunteers (1 man and 12 women), who were students or staff at Wayo Women's University, participated in the study. Each participant took a CoQ_{10} supplement with a meal on four occasions, with the food type containing the CoQ_{10} differing on each occasion. Table 1 shows the meal composition, the sauce of the CoQ_{10}, the nutrient content of the meals. Using the data by Kubo et al. [42], CoQ_{10} content obtained from the meals in the clear soup, miso soup, milk soup, and raw egg source experiments were estimated as 0.52, 0.55, 0.56, and 0.59 mg, respectively, and these were the less than one two-hundredth of the CoQ_{10} supplements ingested. It suggests that the effect of CoQ_{10} content in meals itself was vanishingly low. The number of participants in each experiment is shown in Table S1. Photos of the meal components provided for the subjects are shown in Figure S1. In the experiments, each participant ingested 120 mg of reduced CoQ_{10} (a sachet of P30) suspended in the food (indicated by red arrowheads in Figure S1). In the meals containing P30, the ratio of the concentrations of the reduced form of CoQ_{10} concentration to total coenzyme Q_{10} was >99%. To minimize the number of confounding factors, the same meal was consumed in each experiment, with the exception of the food item containing the P30.

The nutrient content of the meals was estimated using Calorie Make software (Toyo System Science Co., Ltd., Yokohama, Japan). The consumption of the meals started around 12:00 h, at least 3 h after breakfast. The control and test experiments were performed between March and December 2018 at intervals of 6–14 weeks. All subjects gave their informed consent for inclusion before they participated in this study. This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Wayo Women's University Human Research Ethics Committee (no. 1734).

2.3. Blood Collection and CoQ_{10} Measurements. Blood samples were drawn from a vein at the baseline (just before meal ingestion), and 1.5, 3, and 5 h after the start of the meal, and serum was obtained by centrifugation after clot formation. Quantitative analysis of serum CoQ_{10} concentration was measured by Kaneka Techno Research Co., Ltd., using liquid chromatography with tandem mass spectrometry (LC/MS/MS) [43, 44]. In brief, 0.7 mL of the isopropanol was added to 0.1 mL of serum, mixed, and stored at −80°C until just before the analysis. After centrifugation, the supernatant

Table 1: Meal menus for each experiment.

Experiment no.	1	2	3	4
Experiment	Clear soup	Miso soup	Milk soup	Raw egg sauce
Meal menu				
Main dish	Grilled salmon with Japanese radish marinated in citrus juice			
Side dish	Boiled spinach flavored with bonito flakes and soy sauce			
Staple food	Rice	Rice	Rice	Rice with stirred raw egg sauce[a]
Soup	Clear soup[a]	Miso soup[a]	Milk soup[a]	Miso soup
Other	—	—	—	—
Nutrient content per serve				
Energy (kcal)	336	356	437	430
Protein (g)	20.1	21.5	25.1	27.5
Fat (g)	3.6	4.3	9.3	9.4
Carbohydrate (g)	54.1	56.5	61.3	56.4
CoQ_{10} (mg)[b]	120	120	120	120

[a]P30 was suspended in this food item; [b]only CoQ_{10} obtained from P30 is recorded.

was filtered through a membrane filter. Then, 200 μL aliquots were mixed with 200 μL of methanol and 50 μL of oxidized CoQ_9 (50 ng/mL in 2-propanol) as an internal standard and used as the sample for LC/MS/MS, which was performed using an AB Sciex Triple Quad 5500 LC-MS/MS system and a reversed-phase octadecyl-silica column (AB Sciex, Framingham, MA, USA). The intra- and interday coefficients of variation for CoQ_{10} were less than 2 and 10%, respectively.

2.4. Data Analysis. The increase in concentration of CoQ_{10} in the serum after the ingestion of a CoQ_{10}-suspended test meal (ΔCoQ_{10}) was calculated by subtracting the baseline value, and numerical data are expressed as mean ± SD. To compare the bioavailabilities of CoQ_{10}, the areas under the serum CoQ_{10} concentration-time curves up to 5 h after ingestion (ΔAUC_{0-5}) were calculated. These data were analyzed using one-way analysis of variance (ANOVA) with unpaired and repeated measures, and the differences between the means were evaluated by Holm–Bonferroni post hoc testing using js-STAR ver. 9. 3. 0j web application software (http://www.kisnet.or.jp/nappa/software/star/). $P < 0.05$ was considered to represent statistical significance.

3. Results

Thirteen healthy volunteers (1 man and 12 women) participated in the study. Each ingested a CoQ_{10} supplement in the form of suspended a suspension in a food item on up to four separate occasions. Twelve participated in the first experiment (supplemental CoQ_{10} in clear soup as a reference), thirteen participated in the second experiment (supplemental CoQ_{10} in miso soup), nine participated in the third experiment (supplemental CoQ_{10} in milk soup), and thirteen participated in the fourth experiment (supplemental CoQ_{10} in a raw egg sauce). The participation of each individual and the increases in serum total CoQ_{10} concentration after each meal are shown in Tables S1 and S2, respectively. ΔAUC_{0-5} was also calculated for each participant (Table S2).

First, the increase in serum total CoQ_{10} (ΔCoQ_{10}) concentration after each of the four experiments were compared using unpaired one-way ANOVA and Holm–Bonferroni post hoc testing because some participants missed in the first and third experiments. The concentration achieved following the consumption of P30 in miso soup was significantly higher than that achieved following consumption of the raw egg sauce after 1.5 h and higher than that achieved following all three other meals after 3 h (Figure S2A). There were significant differences in ΔAUC_{0-5} between the clear soup and miso soup days, and between the miso soup and raw egg sauce days (Figure S2B). The ΔAUC_{0-5} following miso soup ingestion was 4.44 ± 1.40 μmol h/L, which is approximately 1.5- and 1.6-fold higher ($P < 0.05$) than that on the clear soup (2.97 ± 1.11 μmol h/L) and raw egg sauce (2.84 ± 1.36 μmol h/L) days, respectively (Table S2).

Then, we reanalyzed the data from the eight participants (numbers 3, 4, 5, 8, 9, 11, 12, and 13) who had participated in all of the four experiments (Table S1), using one-way ANOVA with repeated measures (Figure 1). The ΔCoQ_{10} on the miso soup day was significantly higher than on the raw egg sauce days after 1.5 h and higher than on all of the other 3 days 3 h after ingestion (Figure 1(a)). The mean ΔAUC_{0-5} on the miso soup day was 4.94 ± 1.51 μmol h/L, which was 1.6~1.7-fold higher ($P < 0.05$) than that on the clear soup (3.08 ± 1.33 μmol h/L), milk soup (2.95 ± 1.07 μmol h/L), and raw egg sauce (3.05 ± 1.64 μmol h/L) days, respectively (Figure 1(b)).

These results demonstrate that the absorption rate and bioavailability of supplemental reduced CoQ_{10} up to 5 h after ingestion was increased by suspending it in miso soup. However, this effect was abolished when the CoQ_{10} was suspended in raw egg sauce, even if miso soup was ingested at the same time (experiment 4).

4. Discussion

In this study, we determined whether the absorption of a CoQ_{10} supplement would be affected when it was suspended in specific foods. There were no differences in either ΔCoQ_{10} or ΔAUC_{0-5} among participants who consumed a clear soup and test meals on different days, with the exception of the day they consumed the supplement in miso soup. Both the ΔCoQ_{10} at 3 h and the

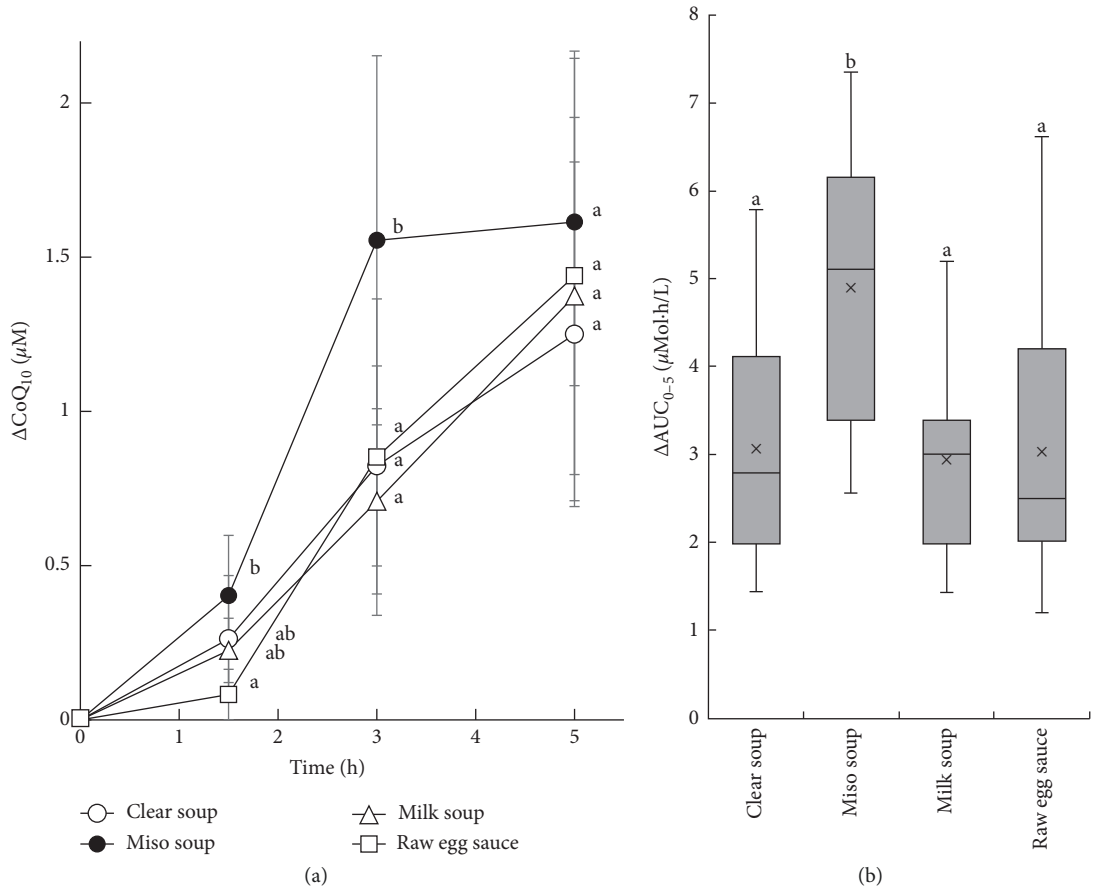

Figure 1: Changes in serum total CoQ_{10} concentration (a) and a comparison of ΔAUC_{0-5} (b) after the consumption of P30 in clear soup, P30 in miso soup, P30 in milk soup, or P30 in raw egg sauce. 120 mg of CoQ_{10} was administered. In Figure 1(a), the open circle represents P30 in clear soup, closed circle represents P30 in miso soup, open triangle represents P30 in milk soup, and open square indicates P30 in raw egg sauce. Data are mean ± SD for the eight individuals who participated in all four of the experiments. Figure 1(b) shows box plots for the ΔAUC_{0-5} for these eight participants. The boundary of the box closest to zero indicates the 25th percentile, the line within the box indicates the median, the multiplication sign within the box indicates the mean, and the boundary of the box farthest from the origin indicates the 75th percentile. Whiskers above and below the box indicate the 10th and 90th percentiles. Data were analyzed with one-way analysis of variance with repeated measures, and differences between the means were evaluated using Holm–Bonferroni post hoc tests. Different lower case letters indicate significant differences, with $P < 0.05$.

ΔAUC_{0-5} for CoQ_{10} after ingestion of the miso soup was significantly higher than after ingestion of clear soup, milk soup, or raw egg sauce (Figure 1(a)). This result suggests that the suspension of P30 in miso soup may be an effective way of increasing the bioavailability of orally administered CoQ_{10}, especially for older people, as the frequency of miso soup consumption is increased with age in Japanese [45].

Interestingly, the effect of miso soup on the absorption of CoQ_{10} was abolished when P30 was suspended in raw egg sauce, despite miso soup also being consumed. This suggests that an interaction between the reduced form of CoQ_{10} and a component of miso might be necessary for the increase in bioavailability of CoQ_{10} achieved by the consumption of miso soup. The absorption of orally administered CoQ_{10} is improved when emulsified with a surfactant that has a higher hydrophile-lipophile balance value [46]. Soy proteins have emulsifying and interfacial properties [47], and the amino-carbonyl reaction of soy proteins with sugar improves their emulsifying properties [48]. Some of the soy proteins in miso are modified by the amino-carbonyl reaction, which explains its brown color. Thus, these modified proteins in miso might be candidates for the components responsible for the enhancement of CoQ_{10} absorption, by emulsification. Besides, miso and soybean extracts improve zinc absorption via increasing cell surface abundance of a zinc transporter [49, 50]. Some components in miso might affect the expression and the activity of a CoQ_{10} transporter protein. However, further studies are required to determine the identity of the active component(s) and the mechanisms involved in the enhanced absorption of CoQ_{10}. The miso used in the present study contained only 3.76 and 0.02 μg of the reduced and oxidized forms of CoQ_{10} per g miso (data not shown), and 10 g of the miso was used for the preparation of one serving of miso soup; therefore, it is unlikely that the CoQ_{10} contributed by the miso is involved in the enhancement in bioavailability of CoQ_{10}.

We also estimated the ΔAUC value for the reduced form of CoQ_{10} in the previously published study to compare these

with the ΔAUC_{0-5} values obtained in the present study. Hosoe et al. performed a single-dose experiment after meal ingestion using 150 mg of the reduced form of CoQ_{10} in a soft capsule [27]. The estimated ΔAUC for the first 6 h after ingestion (ΔAUC_{0-6}) in this study was 2.9 μmol h/L, whereas the ΔAUC_{0-5} in our control experiment, in which 120 mg of the reduced form of CoQ_{10} was consumed in a clear soup was 2.97 ± 1.11 μmol h/L (Experiment 1 in Table S2), suggesting that similar results can be obtained when the reduced form of CoQ_{10} is administered. The ΔAUC_{0-5} associated with P30-plus-miso ingestion (4.44 ± 1.40 μmol h/L, Experiment 2 in Table S2) was >1.5 times higher than those associated with the ingestion of other foods (clear soup, milk soup, and raw egg sauce), implying that the ingestion of CoQ_{10} suspended in miso soup is one of the best ways of increasing its bioavailability, at least, when P30 is used.

One limitation of our study was that the serum concentrations of CoQ_{10} were determined only up to 5 h after ingestion because of the research environment and availability of the participants. In contrast, in most previous studies, these concentrations were determined up to 12 or 24 h after a single dose of CoQ_{10}. One could argue that miso soup may accelerate rather than enhance CoQ_{10} absorption, as the maximum CoQ_{10} concentration or the maximum CoQ_{10} concentration-time could not be determined. The half-life of CoQ_{10} in plasma may reach 33 h, and 5 to 6 days were required for plasma CoQ_{10} levels to return to baseline following a single dose [51]. The possibility of overestimation of the effect of miso soup on CoQ_{10} absorption cannot be denied.

Another limitation of our study was that there is no negative control, i.e., meals alone. In the previous reports, there was no placebo control for the determination of the absorption/bioavailability of CoQ_{10} supplements [25–27, 52–55]. Also, the effect of CoQ_{10} contents in the provided meals seemed to be extremely low as the estimated CoQ_{10} amount was less than one two-hundredth of the CoQ_{10} supplements ingested. However, these remain in a matter of speculation.

To further characterize the effects of miso soup ingestion on the bioavailability of CoQ_{10}, it would be of interest to compare the serum concentrations of CoQ_{10} after multiple meals of miso soup or water containing P30 with or after meals for several weeks. The significance of the present findings will be evaluated by performing such a clinical experiment in the near future.

5. Conclusions

In conclusion, the ingestion of a granulated and reduced form of CoQ_{10} in miso soup increased the bioavailability of CoQ_{10} by ~1.5 times over its ingestion under the other conditions tested. Thus, the absorption of a CoQ_{10} supplement can be enhanced by combining it with specific food substances, such as miso, in addition to taking it with a meal *per se*.

Data Availability

The data used to support the findings of this study are included within the article and also available upon request.

Disclosure

The sponsors had no role in the design, execution, interpretation, or writing of the study.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions

T. S. conceptualized the study; M. T. and T. S. took part in clinical study design, collection of laboratory data, and writing of the original draft; and M. T., M. N., T. K., and T. S. conducted the clinical study and read, revised, and approved the final version of the manuscript.

Acknowledgments

The authors thank Dr. Kenji Fujii of Kaneka Corporation for providing the granulated reduced CoQ_{10} supplement and analyzing the serum CoQ_{10} concentrations. They also thank Ms. Hitomi Kobayashi, Ms. Miku Hatsushiba, and Ms. Ayaka Hanada for their help with meal preparation for the clinical study. Finally, they thank Mark Cleasby, Ph.D., from Edanz Group (http://www.edanzediting.com/ac) for editing a draft of this manuscript. This study was supported by funding from the Kaneka Corporation (Osaka, Japan), on the basis of a contract between Kaneka and Wayo Women's University.

Supplementary Materials

Figure S1: Meals provided to the participants. Figure S2: Changes in serum total CoQ_{10} using unpaired one-way ANOVA. Table S1: Participation in each of the four experiments. Table S2: The increase in serum total CoQ_{10} concentration of each subject after the consumption of each food type. (*Supplementary Materials*)

References

[1] F. L. Crane, "Biochemical functions of coenzyme Q_{10}," *Journal of the American College of Nutrition*, vol. 20, no. 6, pp. 591–598, 2001.

[2] G. López-Lluch, J. C. Rodríguez-Aguilera, C. Santos-Ocaña, and P. Navas, "Is coenzyme Q a key factor in aging?," *Mechanisms of Ageing and Development*, vol. 131, no. 4, pp. 225–235, 2010.

[3] B. Frei, M. C. Kim, and B. N. Ames, "Ubiquinol-10 is an effective lipid-soluble antioxidant at physiological concentrations," *Proceedings of the National Academy of Sciences*, vol. 87, no. 12, pp. 4879–4883, 1990.

[4] A. Kalén, E.-L. Appelkvist, and G. Dallner, "Age-related changes in the lipid compositions of rat and human tissues," *Lipids*, vol. 24, no. 7, pp. 579–584, 1989.

[5] G. Ravaglia, P. Forti, F. Maioli et al., "Coenzyme Q_{10} plasma levels and body composition in elderly males," *Archives of Gerontology and Geriatrics*, vol. 22, no. 1, pp. 539–543, 1996.

[6] M. Takahashi, T. Suzuki, H. Matsumoto, T. Kaneko, H. Nukada, and N. Hashizume, "Decreased blood levels of

L-carnitine and coenzyme Q_{10} in long-term hospitalized people," *New Diet Therapy*, vol. 30, no. 3, pp. 23–33, 2014.

[7] K. Adarsh, H. Kaur, and V. Mohan, "Coenzyme Q_{10}(CoQ_{10}) in isolated diastolic heart failure in hypertrophic cardiomyopathy (HCM)," *Biofactors*, vol. 32, no. 1–4, pp. 145–149, 2008.

[8] J. J. V. McMurray, P. Dunselman, H. Wedel et al., "Coenzyme Q_{10}, rosuvastatin, and clinical outcomes in heart failure: a prespecified substudy of CORONA (controlled rosuvastatin multinational study in heart failure)," *Journal of the American College of Cardiology*, vol. 56, no. 15, pp. 1196–1204, 2010.

[9] Y. Miyake, A. Shouzu, M. Nishikawa et al., "Effect of treatment with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors on serum coenzyme Q_{10} in diabetic patients," *Arzneimittelforschung*, vol. 49, no. 4, pp. 324–329, 2011.

[10] K. Gazdíková, A. Gvozdjáková, J. Kucharská, V. Spustová, Z. Braunová, and R. Dzúrik, "Oxidative stress and plasma concentrations of coenzyme Q," *Nephron*, vol. 88, no. 3, p. 285, 2001.

[11] Y. Yamamoto and S. Yamashita, "Plasma ubiquinone to ubiquinol ratio in patients with hepatitis, cirrhosis, and hepatoma, and in patients treated with percutaneous transluminal coronary reperfusion," *Biofactors*, vol. 9, no. 2–4, pp. 241–246, 1999.

[12] F. L. Rosenfeldt, S. J. Haas, H. Krum et al., "Coenzyme Q_{10} in the treatment of hypertension: a meta-analysis of the clinical trials," *Journal of Human Hypertension*, vol. 21, no. 4, pp. 297–306, 2007.

[13] S. Golbidi, S. A. Ebadi, and I. Laher, "Antioxidants in the treatment of diabetes," *Current Diabetes Reviews*, vol. 7, no. 2, pp. 106–125, 2011.

[14] C. Henchcliffe and M. F. Beal, "Mitochondrial biology and oxidative stress in Parkinson disease pathogenesis," *Nature Clinical Practice Neurology*, vol. 4, no. 11, pp. 600–609, 2008.

[15] M. Moccia, A. Capacchione, R. Lanzillo et al., "Coenzyme Q_{10} supplementation reduces peripheral oxidative stress and inflammation in interferon-β1a-treated multiple sclerosis," *Therapeutic Advances in Neurological Disorders*, vol. 12, Article ID 1756286418819074, 2019.

[16] C. Hofman-Bang, N. Rehnqvist, K. Swedberg, I. Wiklund, and H. Astrom, "Coenzyme Q_{10} as an adjunctive in the treatment of chronic congestive heart failure: the Q_{10} study group," *Journal of Cardiac Failure*, vol. 1, no. 2, pp. 101–107, 1995.

[17] S. Deguchi, K. Fujii, and T. Kurihara, "The effect of the reduced form of coenzyme Q_{10} (ubiquinol, Kaneka QH™) on QOL improvement in the elderly," *Journal of Clinical Therapeutics & Medicines*, vol. 24, no. 3, pp. 233–238, 2008.

[18] R. E. Lister, "An open, pilot study to evaluate the potential benefits of coenzyme Q_{10} combined with Ginkgo biloba extract in fibromyalgia syndrome," *Journal of International Medical Research*, vol. 30, no. 2, pp. 195–199, 2002.

[19] J. Castro-Marrero, M. D. Cordero, M. J. Segundo et al., "Does oral coenzyme Q_{10} plus NADH supplementation improve fatigue and biochemical parameters in chronic fatigue syndrome?," *Antioxid Redox Signal*, vol. 22, no. 8, pp. 679–685, 2015.

[20] J. Castro-Marrero, N. Saez-Francas, M. J. Segundo et al., "Effect of coenzyme Q_{10} plus nicotinamide adenine dinucleotide supplementation on maximum heart rate after exercise testing in chronic fatigue syndrome—a randomized, controlled, double-blind trial," *Clinical Nutrition*, vol. 35, no. 4, pp. 826–834, 2016.

[21] T. Miyamae, M. Seki, T. Naga et al., "Increased oxidative stress and coenzyme Q_{10} deficiency in juvenile fibromyalgia: amelioration of hypercholesterolemia and fatigue by ubiquinol-10 supplementation," *Redox Report*, vol. 18, no. 1, pp. 12–19, 2013.

[22] M. Berman, A. Erman, T. Ben-Gal et al., "Coenzyme Q_{10} in patients with end-stage heart failure awaiting cardiac transplantation: a randomized, placebo-controlled study," *Clinical Cardiology*, vol. 27, no. 5, pp. 295–299, 2004.

[23] A. Monsef, S. Shahidi, and A. Komaki, "Influence of chronic coenzyme Q_{10} supplementation on cognitive function, learning, and memory in healthy and diabetic middle-aged rats," *Neuropsychobiology*, vol. 77, no. 2, pp. 92–100, 2019.

[24] C. Andreani, C. Bartolacci, M. Guescini et al., "Combination of coenzyme Q_{10} intake and moderate physical activity counteracts mitochondrial dysfunctions in a SAMP8 mouse model," *Oxidative Medicine and Cellular Longevity*, vol. 2018, Article ID 8936251, 15 pages, 2018.

[25] A. Barakat, R. Shegokar, M. Dittgen, and R. H. Müller, "Coenzyme Q_{10} oral bioavailability: effect of formulation type," *Journal of Pharmaceutical Investigation*, vol. 43, no. 6, pp. 431–451, 2013.

[26] B. Qin, L. Liu, Y. Pan et al., "PEGylated solanesol for oral delivery of coenzyme Q_{10}," *Journal of Agricultural and Food Chemistry*, vol. 65, no. 16, pp. 3360–3367, 2017.

[27] K. Hosoe, M. Kitano, H. Kishida, H. Kubo, K. Fujii, and M. Kitahara, "Study on safety and bioavailability of ubiquinol (Kaneka QH) after single and 4-week multiple oral administration to healthy volunteers," *Regulatory Toxicology and Pharmacology*, vol. 47, no. 1, pp. 19–28, 2007.

[28] A. Ochiai, S. Itagaki, T. Kurokawa, M. Kobayashi, T. Hirano, and K. Iseki, "Improvement in intestinal coenzyme Q_{10} absorption by food intake," *Yakugaku Zasshi*, vol. 127, no. 8, pp. 1251–1254, 2007.

[29] S. Takeda, M. Kimura, R. Marushima et al., "Mayonnaise contributes to increasing postprandial serum beta-carotene concentration through the emulsifying property of egg yolk in rats and humans," *Journal of Nutritional Science and Vitaminology (Tokyo)*, vol. 57, no. 3, pp. 209–215, 2011.

[30] N. Z. Unlu, T. Bohn, S. K. Clinton, and S. J. Schwartz, "Carotenoid absorption from salad and salsa by humans is enhanced by the addition of avocado or avocado oil," *The Journal of Nutrition*, vol. 135, no. 3, pp. 431–436, 2005.

[31] J. E. Kim, M. G. Ferruzzi, and W. W. Campbell, "Egg consumption increases vitamin E absorption from Co-consumed raw mixed vegetables in healthy young men," *The Journal of Nutrition*, vol. 146, no. 11, pp. 2199–2205, 2016.

[32] M. Bach Kristensen, O. Hels, C. Morberg, J. Marving, S. Bugel, and I. Tetens, "Pork meat increases iron absorption from a 5-day fully controlled diet when compared to a vegetarian diet with similar vitamin C and phytic acid content," *British Journal of Nutrition*, vol. 94, no. 1, pp. 78–83, 2005.

[33] J. R. Hunt, S. K. Gallagher, and L. K. Johnson, "Effect of ascorbic acid on apparent iron absorption by women with low iron stores," *The American Journal of Clinical Nutrition*, vol. 59, no. 6, pp. 1381–1385, 1994.

[34] D. Siegenberg, R. D. Baynes, T. H. Bothwell et al., "Ascorbic acid prevents the dose-dependent inhibitory effects of polyphenols and phytates on nonheme-iron absorption," *The American Journal of Clinical Nutrition*, vol. 53, no. 2, pp. 537–541, 1991.

[35] J. Riedl, J. Linseisen, J. Hoffmann, and G. Wolfram, "Some dietary fibers reduce the absorption of carotenoids in women," *The Journal of Nutrition*, vol. 129, no. 12, pp. 2170–2176, 1999.

[36] S. Samman, B. Sandstrom, M. B. Toft et al., "Green tea or rosemary extract added to foods reduces nonheme-iron absorption," *The American Journal of Clinical Nutrition*, vol. 73, no. 3, pp. 607–612, 2001.

[37] J. D. Cook, M. B. Reddy, J. Burri, M. A. Juillerat, and R. F. Hurrell, "The influence of different cereal grains on iron absorption from infant cereal foods," *The American Journal of Clinical Nutrition*, vol. 65, no. 4, pp. 964–969, 1997.

[38] L. Hallberg, L. Rossander-Hulthen, M. Brune, and A. Gleerup, "Inhibition of haem-iron absorption in man by calcium," *British Journal of Nutrition*, vol. 69, no. 2, pp. 533–540, 1993.

[39] M. Brune, L. Rossander, and L. Hallberg, "Iron absorption and phenolic compounds: importance of different phenolic structures," *European Journal of Clinical Nutrition*, vol. 43, no. 8, pp. 547–557, 1989.

[40] M. Takahashi, T. Kinoshita, K. Maruyama, T. Tanigawa, and T. Suzuki, "Association between diet habits and blood coenzyme Q_{10} levels among residents in Kamijima-cho, Ehime," *The Journal of Wayo Women's University*, vol. 56, pp. 123–132, 2016.

[41] M. Takahashi, T. Kinoshita, T. Kaneko, and T. Suzuki, "Investigation of the influence of dietary habits on serum coenzyme Q_{10} level with long-term CoQ_{10} supplement intake," *The Journal of Wayo Women's University*, vol. 58, pp. 111–118, 2018.

[42] H. Kubo, K. Fujii, T. Kawabe, S. Matsumoto, H. Kishida, and K. Hosoe, "Food content of ubiquinol-10 and ubiquinone-10 in the Japanese diet," *Journal of Food Composition and Analysis*, vol. 21, no. 3, pp. 199–210, 2008.

[43] Y. Uchida, K. Wakimoto, H. Takahashi, and K. Fujii, "The bioavailability of reduced coenzyme Q_{10} water-dispersed powder after a single oral dose," *Japanese Journal of Complementary and Alternative Medicine*, vol. 11, pp. 103–105, 2014.

[44] R. Ushikoshi-Nakayama, K. Ryo, T. Yamazaki et al., "Effect of gummy candy containing ubiquinol on secretion of saliva: a randomized, double-blind, placebo-controlled parallel-group comparative study and an in vitro study," *PLoS One*, vol. 14, no. 4, Article ID e0214495, 2019.

[45] M. Wakasugi, J. James Kazama, and I. Narita, "Associations between the intake of miso soup and Japanese pickles and the estimated 24-hour urinary sodium excretion: a population-based cross-sectional study," *Internal Medicine*, vol. 54, no. 8, pp. 903–910, 2015.

[46] Y. Sato, H. Mutoh, M. Suzuki, Y. Takekuma, K. Iseki, and M. Sugawara, "Emulsification using highly hydrophilic surfactants improves the absorption of orally administered coenzyme Q_{10}," *Biological and Pharmaceutical Bulletin*, vol. 36, no. 12, pp. 2012–2017, 2013.

[47] C. H. Tang, "Emulsifying properties of soy proteins: a critical review with emphasis on the role of conformational flexibility," *Critical Reviews in Food Science and Nutrition*, vol. 57, no. 12, pp. 2636–2679, 2017.

[48] R. Li, X. Wang, J. Liu et al., "Relationship between molecular flexibility and emulsifying properties of soy protein isolate-glucose conjugates," *Journal of Agricultural and Food Chemistry*, vol. 67, no. 14, pp. 4089–4097, 2019.

[49] A. Hashimoto and T. Kambe, "Approaches to the improvement of zinc nutrition by fermented soy foods like miso: effects on expression of zinc transporter involved in zinc absorption in the intestinal epithelial cells," *Journal of the Brewing Society of Japan*, vol. 106, no. 12, pp. 811–817, 2011.

[50] A. Hashimoto, K. Ohkura, M. Takahashi et al., "Soybean extracts increase cell surface ZIP4 abundance and cellular zinc levels: a potential novel strategy to enhance zinc absorption by ZIP4 targeting," *Biochemical Journal*, vol. 472, no. 2, pp. 183–193, 2015.

[51] M. V. Miles, "The uptake and distribution of coenzyme Q_{10}," *Mitochondrion*, vol. 7, no. l, pp. S72–S77, 2007.

[52] G. Lopez-Lluch, J. Del Pozo-Cruz, A. Sanchez-Cuesta, A. B. Cortes-Rodriguez, and P. Navas, "Bioavailability of coenzyme Q_{10} supplements depends on carrier lipids and solubilization," *Nutrition*, vol. 57, pp. 133–140, 2019.

[53] A. Martucci, D. Reurean-Pintilei, and A. Manole, "Bioavailability and sustained plasma concentrations of CoQ_{10} in healthy volunteers by a novel oral timed-release preparation," *Nutrients*, vol. 11, no. 3, 2019.

[54] K. Nukui, T. Yamagishi, H. Miyawaki, A. Kettawan, T. Okamoto, and K. Sato, "Comparison of uptake between PureSorb-Q™40 and regular hydrophobic coenzyme Q_{10} in rats and humans after single oral intake," *Journal of Nutritional Science and Vitaminology*, vol. 53, no. 2, pp. 187–190, 2007.

[55] A. Ozaki, A. Muromachi, M. Sumi, Y. Sakai, K. Morishita, and T. Okamoto, "Emulsification of coenzyme Q_{10} using gum Arabic increases bioavailability in rats and human and improves food-processing suitability," *Journal of Nutritional Science and Vitaminology*, vol. 56, no. 1, pp. 41–47, 2010.