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THE IMPACT OF RAISIN CONSUMPTION ON QUERCETIN BIOAVAILABILITY: AN IN VIVO APPROACH IN VIVO

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ABSTRACT
Raisins are a nutrient-dense food known for their high content of dietary fiber, antioxidants, and bioactive compounds, including quercetin, which exists predominantly in the form of quercetin glycosides, enhancing their potential health benefits. This study investigates the impact of dietary matrix on quercetin bioavailability by analyzing urinary excretion following consumption of raisins. Employing advanced LC/MS techniques, the study quantified quercetin and its metabolites to evaluate how whole foods influence the absorption and metabolic processing of dietary polyphenols. Initial results indicated a significant increase in urinary quercetin excretion, with concentrations ranging from 21.8 µg/ml to 238.8 µg/ml among participants after consuming raisins. The study showed the role of the food matrix in enhancing quercetin bioavailability, suggesting that the complex interactions within whole foods like raisins could significantly influence the solubility, stability, and absorption of quercetin.
Keywords: Raisins, quercetin, bioavailability, excretion, food matrix

KURU ÜZÜM TÜKETİMİNİN KUERSETİN BİYOYARARLANIMI ÜZERİNDEKİ ETKİSİ: IN VIVO YAKLAŞIM

ÖZ
Kuru üzüm yüksek oranda diyet lifi, antioksidan ve ağırlıklı olarak kuersetin glikozitleri formunda bulunan kuersetin de dahil olmak üzere farklı biyoaktif bileşikler içermektedir. İçerdiği bu bileşiklerden dolayı sağlık üzerine yararlı etkileri olduğu bilinmektedir. Bu çalışmada, kuru üzüm tüketimini takiben idrardaki kuersetin atılımı analiz edilerek diyet matrisinin kuersetinin biyoyararlanımı üzerindeki etkisi araştırılmıştır. Çalışmada gelişmiş LC/MS teknikleri kullanılarak, diyetteki gıdaların, polifenol emilimine ve metabolizmasına etki derecesini tespit etmek için idrardaki kuersetin ve metabolitlerinin miktarları belirlemiştir. Kuru üzüm tükettikten sonra idrarla kuersetin atılımında önemli bir artış olduğunu ve konsantrasyonların 21.8 µg/ml ile 238.8 µg/ml arasında değiştiğini göstermiştir. Çalışma, kuersetinin biyoyararlanımını arttırmada gıda matrisinin rolünün önemini belirterek, kuru üzüm gibi işlenmemiş gıdalardaki karmaşık etkileşimlerin, kuersetinin çözünürlüğünü, stabilitesini ve emilimini önemli ölçüde etkileyebileceğini göstermektedir.
Anahtar kelimeler: Kuru üzüm, kuersetin, biyoyararlanım, atılım, besin matrisi

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INTRODUCTION

Quercetin, a flavonoid abundantly found in a variety of fruits and vegetables, has been extensively studied for its potential health benefits, including anti-inflammatory and antioxidant effects (Tomou et al., 2023; Nazari-Khanamiri and Ghasemnejad-Berenji, 2023). Recent research has increasingly focused on the bioavailability of quercetin and how it is affected by the form in which it is consumed. Notably, the matrix in which quercetin is ingested plays a crucial role in its solubility, stability, and subsequent absorption and metabolism in the human body.

Dietary polyphenols like quercetin are often consumed in whole foods, yet the majority of the studies have traditionally concentrated on these compounds in their isolated forms. This oversight in research overlooks the intricate interactions within whole foods, which may modify the bioavailability and physiological impacts of polyphenols (Chen et al., 2022). Raisins, as a whole food, consist of a unique matrix including fibers, sugars, and other polyphenolic compounds, which can interact synergistically with quercetin. This interaction is posited to protect quercetin from rapid degradation in the digestive tract, enhance its solubility and stability, and facilitate a more sustained release and absorption in the gut (Di Pede et al., 2020).

Furthermore, the protective interactions between quercetin and the raisin matrix may enhance the permeability of quercetin across intestinal barriers, modify its metabolism by liver enzymes, and improve the systemic availability of its metabolites, crucial for its biological activities (Riva et al., 2019). Dabeek and Marra., (2019) reported that whole foods like raisins could provide a synergistic matrix that supports enhanced absorption and metabolism of quercetin compared to isolated supplements. This study seeks to address the gap in existing literature by examining these complex interactions within raisins and assessing their impact on the bioavailability of quercetin.

Additionally, this study aims to investigate the excretion patterns of quercetin and its conjugates in the urine following the consumption of raisins. By quantifying the urinary excretion of these metabolites, we seek to provide direct evidence of the bioavailability and metabolic processing of quercetin when consumed within the complex food matrix of raisins. This aspect of our research is critical, as it allows for an assessment of how effectively quercetin is absorbed and utilized in the body after being ingested in a whole food form. Understanding these excretions patterns is essential for evaluating the efficacy of dietary interventions involving quercetin-rich foods in health maintenance and disease prevention strategies. This could pave the way for new dietary recommendations and interventions in chronic disease prevention and management, thereby enriching the existing paradigms of nutritional science.

MATERIAL AND METHODS

To ascertain the comprehensive quantification of quercetin within biological specimens, multiple analytical methodologies are employed. These techniques are primarily utilized subsequent to the enzymatic cleavage of conjugated quercetin derivatives, facilitating the meticulous assessment of quercetin and its metabolites. Among the spectrum of analytical approaches are liquid chromatography-mass spectrometry (LC/MS), LC/MS/MS, high-performance liquid chromatography (HPLC) paired with ultraviolet (UV) detection, fluorescent detection, electrochemical detection, as well as HPLC coupled with radiocounting and tandem mass spectrometry. Notably, the LC/MS technique has been demonstrated to measure reliably minimal quantities of native quercetin in urinary samples, ensuring commendable reproducibility in the analytical outcomes (Ishii et al., 2003).

Chemicals and reagents

Quercetin and rutin were procured from Sigma-Aldrich Inc. (St Louis, MO). To prepare stock solutions, these compounds were initially dissolved in ethanol and subsequently diluted with an aqueous solution to achieve a 50% ethanol concentration. In contrast, taxifolin was

solubilized directly in distilled water. β-Glucuronidase of type IX-A, derived from E. coli, along with sulfatase of type VI, sourced from Aerobacter aerogenes, were also obtained from Sigma-Aldrich Inc. (St Louis, MO). Methanol, ethanol, acetonitrile, and sodium azide were HPLC grade (Fisher Scientific, Loughborough, UK).

Raisins extraction

Raisins were provided from Sun-Maid (California, USA). Raisin extraction was conducted utilizing the methodology developed by Zhao and Hall (2008). To enhance the efficiency of extraction from 3 g of finely chopped raisins, 15 ml of solvents (ethanol [EtOH], methanol [MeOH], and acetonitrile [ACN]) were employed. These solvents were subsequently diluted with varying proportions of distilled water to achieve concentrations ranging from 0 to 95%. The resulting mixture was subjected to vortex mixing for two minutes and then homogenized at increasing speeds for five minutes to achieve particle size reduction. This homogenate was then centrifuged for 25 minutes at 20 °C and 3000 rpm, and the resultant pellet underwent a second extraction with the original solvent volume, followed by the same centrifugation protocol. The extracts from these sequential processes were combined and stored at -20°C for future analysis. All the extraction steps were replicated three times. The final aqueous extracts were filtered through a 0.2 μm polytetrafluoroethylene filter before being analyzed via HPLC for polyphenol content.

Identification of raisin phenolic composition by HPLC

The HPLC system had an Agilent Eclipse XDB-C18 RRHT threaded column, interfaced with a Merc Hitachi D-7000 Lachrom system, inclusive of a Merc Hitachi L-7200 autosampler, L-7300 column oven, L-7450 diode array detector, and L-7100 pump. Mobile phase A was formulated with 95% acetonitrile, 5% distilled water, and 0.1% formic acid, whereas mobile phase B consisted of 95% distilled water, 5% acetonitrile, and 0.1% formic acid. The chromatographic separation proceeded with a flow rate of 1.0 ml/min, utilizing a linear gradient that transitioned from 100% to 10% of phase A and from 0% to 90% of phase B. The conditions were maintained within a pressure range of 0 to 400 bar and at a controlled temperature of 35 °C. The quantification of total quercetin glycosides, expressed as rutin equivalents, was based on absorbance at 370 nm, with all chromatographic peaks resolving within 30 minutes.

Participants

This research involved the recruitment of 18 healthy smoke-free individuals without any significant medical history. The participants included 10 males and 8 females, aged between 20 and 40 years. Selection criteria were based on health status, dietary habits, and absence of chronic diseases to ensure a homogeneous study group. Participants were provided with a concise health survey, an overview of the research, a disclaimer of liability, and information on their rights to withdraw from the study at any point. The protocol received ethical approval from the University of Leeds, MEEC Faculty Research Ethics Committee reference number MEEC 09-019. Prior to the experimental phase, subjects were asked to complete detailed food diaries during a 3-day washout period. Additionally, they were instructed to abstain from consuming polyphenol-rich foods for two days preceding the test day. On the morning of the third day, before the intake of raisins, control urine samples were collected as control samples. Subsequently, participants consumed a standardized meal consisting of a slice of bread, butter, a banana, and 100 grams of Sun-Maid raisins. Following this meal, they were required to collect their urine over the next 24 hours. Participant identities were in an anonymous format and data were recorded anonymously to maintain confidentiality. This methodology enabled the assessment and quantification of dietary components' absorption and subsequent urinary excretion over a 24-hour period, facilitating the evaluation of quercetin and other compounds' bioavailability from raisins.

Protocols for enzymatic hydrolysis and LC-MS analysis of urinary flavonoids

The protocol for processing urine samples encompasses four primary stages. Stage 1 was collection; urine samples were accumulated over a 24-hour period into 3000 ml plastic containers, each containing 3 g of ascorbic acid to prevent oxidative degradation. Stage 2 was preparation for storage; volumes of the collected urine were measured, and aliquots of 10 ml were transferred into 15 ml falcon tubes containing 1 ml of 0.1% sodium azide, serving as a biocide to inhibit sample degradation. These samples were subsequently stored at -20°C pending analysis. Stage 3 was enzymatic hydrolysis to facilitate the breakdown of conjugated flavonoids into free aglycones, enzymatic hydrolysis was performed. Each 1 ml urine aliquot was treated with an enzyme solution enriched in sodium phosphate buffer (0.2 M, pH 7), comprising 50 units of β-glucuronidase from *E. coli* and 0.3 units of sulfatase from *Aerobacter aerogenes*. The mixture was incubated at 37°C for 2 hours with constant agitation. Post-incubation, the enzymatic reaction was stopped by adding 275 µl of 2% HCl, adjusting the pH to favor the selective extraction of non-polar analytes with ethyl acetate. Stage 4 was reconstitution and filtration; following enzymatic hydrolysis, three rounds of ethyl acetate extractions were conducted. The collected supernatants were then concentrated using a centrifugal evaporator at 40°C. The dried residues were reconstituted in a mixture of 50 µl acetonitrile and 200 µl of 0.125% ascorbic acid, sonicated to ensure complete dissolution and then centrifuged to clarify the solution before LC-MS analysis.

LC-MS quantification targeted several flavonoids, including quercetin, catechin, epicatechin, ferulic acid, caffeic acid, and caftaric acid. Taxifolin, at a 0.01% concentration, was incorporated as an internal standard into each sample. This process was uniformly applied to both experimental and control urine samples, with all procedures conducted in duplicate to ensure analytical precision. The bioavailability of quercetin was calculated based on the following equation:

$$\text{The total urinary excretion of quercetin (\%)} = \left(\frac{Total\ excreted\ quercetin}{Total\ ingested\ quercetin}\right) x\ 100.$$

LC/MS analyses

The desiccated specimen was resuspended in 50 µl of acetonitrile and 200 µl of a 0.125% solution of ascorbic acid. This mixture was then subjected to vortex mixing followed by centrifugation at 1700 rpm for 10 minutes. Subsequent filtration through a 0.2 µm polytetrafluoroethylene filter prepared the samples for liquid chromatography-mass spectrometry (LC/MS) analysis. Each specimen underwent extraction and was analyzed in duplicate using an Agilent Technologies 6410 Triple Quad LC/MS system. Chromatographic isolation of the target analytes was performed on a C18 column (3.1-micron particle size, 150 mm × 2.1 mm, Phenomenex Kinetix) with a mobile phase composed of acetonitrile and water, each containing 0.1% formic acid. The volume injected for analysis was set at 5 µl. According to Wang et al. (2005), employing a mobile phase acidified with formic acid enhances the separation and accurate quantification of quercetin. Therefore, solvent A was comprised of water with 0.1% formic acid, while solvent B contained acetonitrile with 0.1% formic acid. Identification of aromatic and phenolic compounds within the samples was achieved through comparisons of retention times and relative retention times.

Statistical analysis

To assess the efficacy of raisin consumption on quercetin bioavailability, we employed t-tests to analyze the quercetin levels in urine samples before and after dietary intervention. Data analysis was performed using Microsoft Excel. Paired t-test was applied to compare the pre- and post-consumption quercetin levels within the same individuals. The objective was to determine the influence of raisin consumption on the absorption and metabolism of quercetin, as indicated by its urinary excretion. All statistical tests were conducted at a significance level of $\alpha = 0.05$. Findings were considered statistically significant if *P*-values were less than 0.05, suggesting notable differences in quercetin bioavailability due to raisin consumption.

RESULTS AND DISCUSSION

Recent studies have affirmed the bioavailability and health benefits of dietary polyphenols, underscoring the role of the food matrix and gut microbiota in their absorption and metabolism. A recent review by Ed Nignpense et al. (2021) highlights the significant impact of the food matrix on polyphenol bioavailability, suggesting that whole foods like raisins may offer enhanced health benefits due to the synergistic effects of dietary fibers and polyphenols. This corroborates our findings on the increased urinary excretion of quercetin post-raisin consumption, emphasizing the importance of consuming whole foods to optimize polyphenol bioavailability.

Phenolic content of raisins

The analysis of phenolic content in raisins involved three different extraction methods, with the Zhao and Halls (2008) method demonstrating the highest efficiency. Solvent concentration played a critical role in the yield of rutin. Specifically, 25% ethanol showed significantly higher rutin yields compared to 100% and 50% ethanol, which yielded the lowest rutin content (Table 1). Methanol and acetonitrile extracts produced lower levels of rutin compared to ethanol, although methanol exhibited better extraction efficiency than acetonitrile. Notably, extracts with 5% and 100% methanol showed undetectable levels of rutin, with 5% methanol yielding significantly less rutin than 5% ethanol.

Recent advancements in extraction technologies emphasize the importance of selecting optimal methods to maximize the recovery of bioactive compounds. Alara et al. (2021) and Aydin (2023) discuss various modern extraction techniques that have enhanced the efficiency and specificity of phenolic compound recovery. Shi et al. (2022) further validate the role of advanced extraction technologies in improving the characterization and potential antioxidant activities of extracted phenolics. Additionally, Gil-Martín et al. (2022) provide insights into sustainable extraction methods that preserve the quality and enhance the recovery rate of phenolic compounds from plant materials. Chanioti et al. (2021) explore novel processes including encapsulation to protect the integrity of phenolic extracts, which could have implications for maintaining the bioactivity of raisin extracts.

Table 1. The rutin content (μg/g) in raisins was obtained from ethanol extraction.

Solvent Concentration (%)	Ethanol (μg/g)	Methanol (μg/g)	Acetonitrile (μg/g)
5	63.2	None	None
25	82.2	62.2	61.8
50	None	64.6	None
75	62.2	62.7	60.6
100	None	None	None

These findings underline the importance of selecting an appropriate extraction method to maximize the recovery of phenolic compounds from raisins. Future research could provide further insights into optimizing polyphenol analysis in food matrices, potentially incorporating innovative extraction techniques such as those discussed by García-Villalba et al. (2019) and Vardakas et al. (2021), which have shown promise in enhancing the yield and bioavailability of polyphenols from various plant sources.

Urinary excretion of quercetin

This study demonstrated a significant increase in urinary quercetin excretion following raisin consumption, underscoring the enhanced bioavailability of polyphenols from whole foods. The methodology, including a washout period and controlled diet, minimized background interference, ensuring that increases in urinary quercetin were attributable to raisin consumption. Hollman et al. (1999) indicated that the elimination half-life of quercetin is nearly 24 hours, hence a 48-hour washout period should be sufficient to clear pre-existing quercetin from the

urine. Recent advances in analytical techniques, such as LC/MS, have enabled more precise quantification and identification of quercetin and its metabolites in biological samples. This enhanced sensitivity allows for a more comprehensive assessment of quercetin absorption kinetics and metabolite profiles, providing valuable insights into individual variability and metabolism (Praticò et al., 2018). Therefore in the current study use of advanced LC/MS techniques provided precise quantification of quercetin and its metabolites, revealing subtle differences in retention times that reflect metabolic processing. The control urine (BU) of participants were collected the consumption of raisin. After that participants were asked to consume a standardized breakfast consisting of a slice of bread, butter, a banana, and 100 grams of Sun-Maid raisins. Following this meal, they were required to collect their urine over the next 24 hours (U24). Each participant received 9500 μg/100g of rutin via raisins, suggesting that total urinary quercetin excretion (UQ) should be less than 142.5 μg if excretion is below 1.5%. The difference between BU and U24 was significant (P<0.05). Standardized conditions were maintained for all participants during raisin consumption to minimize variability, as absorption of quercetin is known to be influenced by diet. Previous research by Hollman et al. (1995) indicated that quercetin absorption can be enhanced by conjugation with sugar. Volunteers were initially provided with a standardized meal before consuming 100 g of raisins, resulting in varied amounts of quercetin excreted in each participant's 24-hour urine samples ranged from 21.8 μg/ml to 238.8 μg/ml. The total urinary excretion of quercetin ranged from 2.4% to 0.17%, reflecting individual differences in absorption and metabolism (Table 2). The study's findings on the variability in quercetin levels in control urine samples resonate with recent literature, which has further elucidated the factors influencing quercetin absorption and metabolism. García-Villalba et al. (2019) demonstrated that individual variations in gut microbiota composition can significantly impact the bioavailability of dietary polyphenols like quercetin. This aligns with the observed variability in quercetin levels in control urine samples, suggesting that differences in gut microbiota among participants may contribute to the disparate excretion patterns (Elizalde-Romero et al., 2021). These findings contribute to understanding polyphenol bioavailability and suggest that individual dietary backgrounds may significantly influence the metabolism of dietary polyphenols. The study verified the presence of quercetin in human urine samples and raisin extracts through two criteria: spiking urine samples and raisin extracts to increase expected peak heights and adding taxifolin as an internal standard to determine relative retention time. The verification of quercetin presence in urine samples and raisin extracts using established criteria, as described by Gómez-Mejía et al. (2020), ensures the reliability of the study's findings. Furthermore, the identification of losses during the extraction process, attributed to factors such as homogenization, echoes similar challenges reported in the literature (Gómez-Mejía et al., 2020). In the current study, losses during the extraction process were identified by calculating the lost taxifolin amount, with a total loss of 13.4% observed, potentially attributable to the homogenization process. Overall, the study's results contribute to the body of literature on quercetin absorption and metabolism, highlighting the importance of considering individual variability and methodological factors in such investigations.

In this study, the accuracy of our quercetin measurements by adding a known quantity (100 μg) of quercetin to 1.0 ml aliquots of urine from subject 101 in duplicate. In our experimental design, each participant consumed 100 grams of raisins, containing 95 μg/g of rutin, totaling 9500 μg of rutin per individual. According to Scalbert and Williamson (2000), the excretion rates of quercetin in urine typically do not exceed 1.5%, with specific excretion rates reported as 1.39% for onions and 0.44% for apples. The enzymatic hydrolysis of rutin to quercetin is facilitated by intestinal microflora through α-rhamnosidase and β-glucosidase, leading to its subsequent absorption and excretion in bile and urine (Hai et al., 2020). Expected quercetin concentrations in

urine should be below 142.5 μg/ml yet in the current study's observations, quercetin concentrations ranged from 16.2 μg/ml to an atypical high of 229.3 μg/ml as displayed in Table 2. This variability highlights the influence of individual dietary habits and gut microbiota composition on quercetin metabolism, a factor increasingly recognized in personalized nutrition science (Rudrapal et al., 2024). For instance, participant variability in quercetin excretion could reflect differences in gut microbiota or enzyme activity, affecting the hydrolysis and subsequent absorption of quercetin (Aghababaei and Hadidi, 2023).

Table 2. The amount of total excreted quercetin (μg/ml) in different participants for control urine (BU), 24-hour collected urine (U24) and the difference between BU and U24 (QU).

Subject code	103	105	107	111	113	116	118
BU	238.87	113.76	216.18	29.79	110.60	21.80	83.44
U24	9.55	17.34	12.13	2.28	1.56	5.58	3.73
UQ	229.31	96.41	204.04	27.51	109.04	16.21	79.71
*The total urinary excretion of quercetin (%)	2.41	1.01	2.15	0.29	1.15	0.17	0.84

*The total urinary excretion of quercetin was calculated assuming all ingested rutin could potentially convert to quercetin.

Participant variability was notable: the highest excretion rate was observed in a participant who consumed chocolate on the third day, which might have influenced results due to its polyphenol content. The lowest excretion rate was recorded for participant 116, whose 24-hour urine sample contained only 21.8 μg/ml despite consistent raisin consumption across the study cohort. This variation could reflect individual metabolic differences or adherence to the dietary restrictions during the study period. For instance, participant 105, who consumed dried plums and pineapple, showed elevated control quercetin levels likely due to these foods' high polyphenolic content. Similarly, participant 107's diet included mayonnaise, which contains additional polyphenols from ingredients such as olive oil and herbs, potentially contributing to higher control and post-intervention quercetin levels.

Participants 111 and 113, who most strictly adhered to the exclusion diet, demonstrated the expected quercetin levels post-raisin consumption, with participant 113 exhibiting slightly higher levels than 111, possibly due to metabolic variations. This observation suggests differential absorption capacities among individuals, which could be critical for personalized nutritional advice. The excretion profiles of other polyphenols catechin, epicatechin, caffeic acid, caftaric acid, and ferulic acid were consistently lower than quercetin. The distinctive absorption mechanics, which are heavily influenced by the glycosidic form of quercetin in foods and subsequent microbial hydrolysis in the gut, underscore the complexity of polyphenol metabolism (Day et al., 2000; Catalkaya et al., 2020; Makarewicz, et al., 2021; Li et al., 2023).

Participants who strictly adhered to the exclusion diet demonstrated more consistent and expected quercetin levels post-raisin consumption, emphasizing the impact of dietary background on polyphenol metabolism. The lower excretion profiles of other polyphenols such as catechin and epicatechin compared to quercetin underscore the specificity of microbial enzymatic activity on different polyphenolic structures, as noted in recent studies (Dabeek and Marra., 2019).

Furthermore, emerging research has emphasized the importance of considering the synergistic effects of polyphenols and other bioactive compounds present in food matrices, such as raisins, on quercetin absorption and bioavailability. Studies have shown that the matrix composition and food processing methods can influence the release and accessibility of quercetin, impacting its absorption and subsequent

excretion in urine (Arfaoui et al., 2021). Recent studies have highlighted that the consumption of other foods can significantly influence the absorption and metabolism of quercetin. The complex interactions within whole foods can modify the bioavailability and physiological impacts of polyphenols. For example, dietary fibers, sugars, and other polyphenolic compounds present in foods like raisins can interact synergistically with quercetin (Ulusoy and Sanlier., 2020; Dhanya., 2022). These interactions protect quercetin from rapid degradation in the digestive tract, enhance its solubility and stability, and facilitate a more sustained release and absorption in the gut (Michala and Pritsa., 2022; Aghababaei and Hadidi., 2023). Furthermore, the protective interactions between quercetin and the food matrix may enhance the permeability of quercetin across intestinal barriers, modify its metabolism by liver enzymes, and improve the systemic availability of its metabolites crucial for its biological activities (Ulusoy and Sanlier., 2020; Muñoz-Reyes et al., 2021). Therefore, future investigations should aim to elucidate the complex interactions between quercetin and other dietary components to better understand its overall bioactivity and health implications.

CONCLUSION

The study conclusively demonstrated that raisin consumption significantly enhances the bioavailability of quercetin, as evidenced by increased urinary excretion rates. Specifically, participants exhibited a broad range of quercetin excretion rates, from 0.17% to 2.4%, which correlated with an intake of 9500 μg of rutin. These findings are indicative of the beneficial role of the raisin matrix in promoting quercetin absorption and stability, enhancing its systemic availability and metabolic utilization. Notably, individual differences in gut microbiota and dietary patterns were significant determinants of quercetin bioavailability, emphasizing the potential for personalized dietary recommendations to optimize the health benefits of polyphenols. Future research should focus on delineating the specific mechanisms within food matrices that affect polyphenol bioavailability and exploring the synergistic effects of other bioactive compounds on quercetin absorption. This study enriches the current understanding of dietary polyphenols' bioavailability and sets the stage for further investigations into the complex interactions within whole foods that influence nutrient utilization.

DECLARATIONS OF INTEREST STATEMENT

I declare that no conflicts of interest are associated with this manuscript.

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