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(Poly)phenol profiles of plant-based diets assessed through dietary intake and urinary biomarkers

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(Poly)phenols are bioactive compounds widely present in plant-based foods. The aim was to explore differences in (poly)phenols based on dietary intake and urinary measurements among omnivores and different types of plant-based diets (PBDs). A total of 792 participants completed a 175-item food frequency questionnaire; 200 (51% PBD followers) provided first-morning urine samples. The Phenol-Explorer database was used to estimate dietary (poly)phenol intake. Food contributions to total (poly)phenols and a (Poly)Phenol-rich diet Score (PPS) were assessed. Urinary total (poly)phenols and concentrations of 28 (poly)phenols were quantified using liquid chromatography-tandem mass spectrometry. Diet groups were compared using the Kruskal–Wallis test. Principal component analysis and Spearman's correlation were performed to explore associations between dietary and urinary (poly)phenols. Total and individual (poly)phenol intakes were higher for PBDs compared to omnivores. Among vegans, vegetables (20.8%) and fruits (10.4%) were the main contributors to total (poly)phenols; this pattern was reversed in the other groups. Significant differences ($p < 0.001$) were also observed in the contribution of other plant-based foods, resulting in distinctive profiles across diet groups. PBDs scored higher in the PPS and showed the highest intake and urinary values of isoflavonoids (e.g., vegans: 94 mg per 2000 kcal per day and 1424 ng mL⁻¹, respectively). Genistein and daidzein levels were strongly correlated with their intake values ($\rho \sim 0.6$), as well as with legumes and soy-rich foods. A cluster driven by urinary isoflavonoids was identified. Both dietary and urinary (poly)phenols predominated in PBDs. Genistein and daidzein represent stable biomarkers of legume and soy intake and are key indicators of plant-based dietary patterns.

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1. Introduction

(Poly)phenols are a heterogeneous group of plant-based (PB) metabolites most commonly found in fruits, vegetables, cocoa, and plant beverages such as tea, coffee, wine, and beer. They are considered bioactive compounds with antioxidant and

anti-inflammatory potential, with known preventive effects against cardiovascular and neurodegenerative diseases, and some types of cancer.¹ (Poly)phenols encompass flavonoids (the largest class), phenolic acids, lignans, stilbenes and other compounds. While there are more than 10 000 different individual compounds, around 500 phenolic compounds are the

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most explored in dietary studies, of which flavonoids and phenolic acids each account for 45% of the total.^{2,3}

Dietary intake of (poly)phenols can be estimated through dietary questionnaires along with food composition databases of (poly)phenols such as the Phenol-Explorer and USDA databases.⁴ Food frequency questionnaires (FFQ) do not account for all possible food sources of (poly)phenols due to the limited number of food items. This drawback can be only mitigated by the use of FFQs with an extended list of PB foods, or those that have been developed with the intention of assessing (poly)phenol intake.^{5,6} Once ingested, (poly)phenols present relatively low absorption rates and limited bioavailability depending on the chemical structure (*e.g.*, mean bioavailability for monomer flavan-3-ols is approximately 30%, with a time to reach the maximum plasma concentration of 5.3 hours).⁷ Urinary (poly)phenols may therefore provide a more objective measurement of the dietary exposure, particularly when 24 hour urine is collected, but also when relied on first-morning urine.⁸ Thus, the combination of both dietary and urinary (poly)phenols would provide valuable data to characterize (poly)phenol profiles associated with dietary patterns.⁹

Widely endorsed public health recommendations advocate for reducing meat and other animal-based products to minimize environmental impact and improve population health.^{10–12} This has accelerated the dietary transition towards plant-based diets (PBDs), within which vegetarians, vegans, flexitarians, and pro-vegetarians co-exist. The latter are omnivores who do not restrict, but limit animal food intake, while mostly consuming PB foods. Pro-vegetarians were first defined in 2014 by means of the pro-vegetarian food index,¹³ for which a higher adherence has been related to lower cardiovascular disease and all-cause mortality.¹⁴ Self-identified flexitarians consume animal-based foods occasionally, while vegetarians restrict meat intake, and vegans refuse to consume any animal-based food but preferably consume legume and soy-derived foods as main food sources of proteins.¹⁵ Given that the consumption of PB foods varies by type of diet, differences in the (poly)phenol profiles are expected.

A previous study conducted in the Adventist cohort described (poly)phenol intakes according to the PBD type.¹⁶ However, this population was North American and had specific cultural habits, which limits the generalizability to other populations. Within the European Prospective into Cancer and Nutrition (EPIC) study, an analysis of the dietary intake of (poly)phenols was undertaken, with results being presented for a healthy conscious subcohort comprised of vegetarian and vegan participants.^{3,17} This study collected dietary data at the end of the 1990s and therefore does not reflect current dietary habits, including new PB foods that have since become available in the market. Also, differences by types of PBDs were not accounted for. Moreover, no studies to date have explored biomarker data of these compounds in relation to PBDs, nor (poly)phenol intake of the pro-vegetarian dietary pattern. Therefore, the characterization of PBDs according to dietary (poly)phenols remains unexplored.¹⁸

The OMIVECA study is an ongoing study aimed at characterizing PBDs according to dietary factors. The present study

aimed to compare dietary and urinary (poly)phenol profiles between PBDs and non-PBDs, and across PBD subtypes (vegan, ovo-lacto-vegetarian, pesco-vegetarian, and pro-vegetarian).

2. Methods

2.1 Study population

This cross-sectional study included 864 individuals with complete dietary data (Fig. 1). Participants with implausible total energy intakes (<1200 or >4500 kcal day⁻¹) were excluded ($n = 72$). Among the remaining 792 participants (32.6% PBD followers), 585 were university students or staff in health-related disciplines, particularly of Human Nutrition, recruited from the Universities of Granada, Madrid, Seville, and Almería (Spain). An additional 207 individuals from the general population were included across these centers and other Spanish regions to enhance representativeness and external validity. Recruitment was conducted *via* university booths, academic events, and snowball sampling. A total of 267 participants provided first-morning urine samples, of whom 200 (50% being PBD followers, matched to omnivores by sex, age ± 5 years, center and timing of urine sample collection ± 1 week) were selected for analyzing (poly)phenol biomarkers. Thereby, we included PBD followers and omnivores with higher intake of animal-based foods, to ensure inclusion of participants at the lowest and highest levels of dietary exposure.

All participants provided written informed consent prior to enrollment. The study was approved by the Ethics Committees of Granada and the Autonomous Community of Andalusia (11/21 CEIM/CEI Provincial Granada), the Institute of Health Carlos III ISCIII (CEI/PI/32_2023), the Spanish National Research Council CSIC (2014/2023), and the International Agency for Research on Cancer IARC (IE-2024-4243).

2.2 Data collection

Demographic and lifestyle data (age, sex, height and weight, smoking and alcohol consumption) were collected. Body mass index (BMI) was calculated for each participant. Participants self-identified their dietary pattern as omnivores, vegans, ovo-lacto-vegetarians and pesco-vegetarians. Supplement use was declared by a yes/no question as well as by specifying the supplement name.

2.3 Dietary assessment

Habitual diet over the previous year was assessed between April 2023 and October 2025 through an online semi-validated FFQ of 175 items, implemented in REDCap software.¹⁹ The instrument was derived from a previously validated 137-item Spanish FFQ,²⁰ adding whole grain cereals (wheat pasta, brown rice), berries, types of tea, and 31 other food items considering new PB foods, such as PB beverages and PB meat alternatives. These items were selected based on a review of PB foods on the Spanish market²¹ and expert consensus.

Consumption frequency, ranging from “never or less than once per month” to “six or more times per day”, was trans-



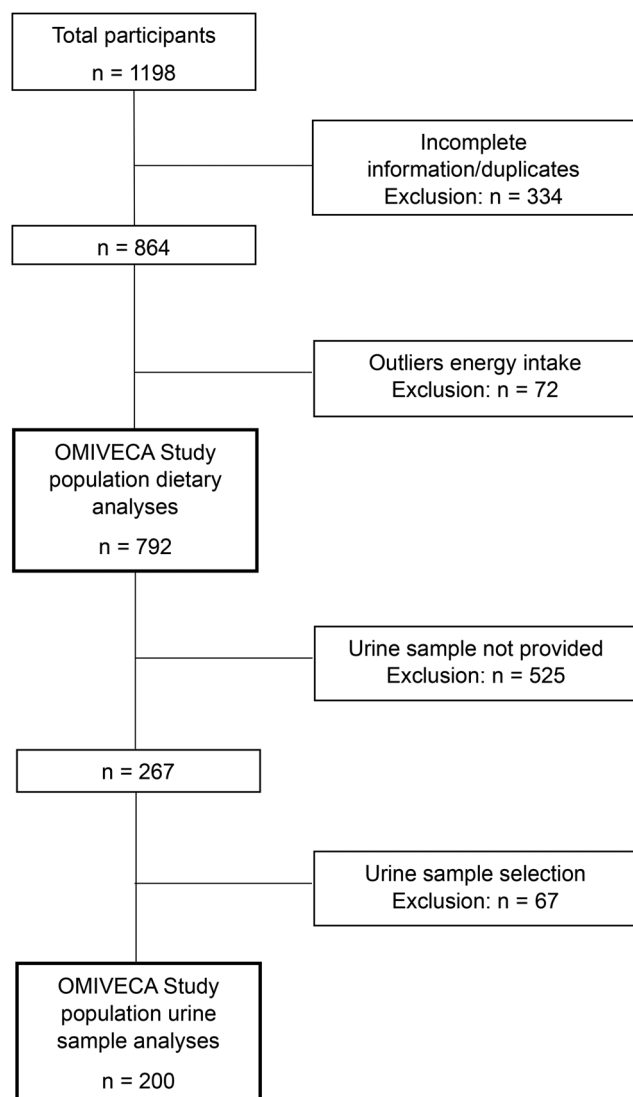


Fig. 1 Flow diagram of the study population. It represents the flow scheme of the population study selection.

formed into estimated daily intakes expressed in grams per day according to portion sizes; most of them were specified within the questionnaire items (Table S1). Seasonal food frequency intakes were corrected by multiplying by a factor depending on the months per year when the foods are available: 0.08 for 1 month per year (*e.g.*, nougat and marzipan), 0.17 for 2 months per year (*e.g.*, cherries and plums), 0.25 for 3 months per year (*e.g.*, strawberries, melon, watermelon and ice cream), and 0.5 for 6 months per year (*e.g.*, oranges).

Food intakes were energy-adjusted to a reference intake of 2000 kcal. Total energy intake was previously derived from the Spanish Food Composition Database BEDCA²² and, when needed, the USDA Food Composition Database was used.²³ Food items were grouped into 28 (poly)phenol-rich food subgroups, further classified into 13 broader food groups (Table S2). Most common (poly)phenol subclasses present in those food groups are detailed in Table S3.

The healthy plant-based diet index (hPDI), a measure of the pro-vegetarian diet, was calculated with 18 food groups, as described elsewhere.²⁴ In brief, each food group was divided into quintiles of intake and classified as animal-based food, and healthy or unhealthy PB food. Afterwards, intake of healthy PB food groups was scored from 1 to 5, from lowest to highest frequency consumption; animal-based foods and unhealthy PB foods were scored reversely (5 to 1). The score was divided into two main categories of adherence: “high” for 64 points or more, and “low-medium” for 63 or less points, from a theoretical maximum range of 90. The fifth diet group of pro-vegetarians was defined as those omnivores with a hPDI ≥ 64 .

2.4 (Poly)phenol dietary intake

Each FFQ item was matched to a food included in the Phenol-Explorer version 3.6 database.²⁵ When a food item could not be clearly identified in this database, matching was performed based on its main compositional ingredients (*e.g.* for guacamole, we considered 70% avocado, 20% tomato and 10% onion; for bakery/pastries, 40% flour and 20% sunflower oil, *etc.*). Foods or ingredients not included in Phenol-Explorer were excluded from the analysis (*e.g.* mushrooms, quinoa, seitan, seaweed, chips and snacks, canned fruits, honey, kefir, mustard and sauces, and vegan precooked meals). During data compilation, total (poly)phenol content (g per 100 g of food) was obtained by summing the amounts contributed by each ingredient. For FFQ items with more than one component, a weighted mean was calculated (*e.g.* (poly)phenols per 100 g of the eggplant-zucchini-cucumber FFQ item were calculated as the mean of the corresponding values for eggplant, zucchini, and cucumber). Finally, of the 175 food items included in the FFQ, (poly)phenol values were assigned to 108 foods available in Phenol-Explorer (Table S4). This allowed us to estimate a total of 396 (poly)phenols. Dietary intake of these (poly)phenols was grouped into 29 subclasses (Table S3), and the dietary intake of total (poly)phenols was calculated *via* the sum of all individual (poly)phenols.

Concerning food groups (Table S2), their contribution was calculated by dividing their (poly)phenol content by total dietary (poly)phenol intake and expressing the result as a percentage. The sum of the contributions of the main groups accounts for approximately 90% of the total.

2.5 (Poly)phenol-rich diet score (PPS)

The PPS was calculated as described by Xu *et al.* 2023,⁵ considering 20 components, with some minor adaptations: tea included black and green tea, along with other infusions; coffee and decaffeinated coffee were grouped; pear and apple were combined; apple juice was replaced by “other natural juices”; and grape juice was added to the grape component. For each component, participants in the highest quintile scored 5 points, whereas those in the lowest scored 1 point. The overall score ranged from 20 to 100.



2.6 Laboratory measurements

First-morning urine was collected to reflect overnight accumulated (poly)phenol concentrations. Samples were kept refrigerated until delivery and stored in a $-80\text{ }^{\circ}\text{C}$ freezer. Total (poly)phenols were measured at the University of Granada, whereas individual (poly)phenols were determined at the IARC.

2.6.1 Total urinary (poly)phenol quantification. Total urinary concentrations were determined using the rapid Folin-Ciocalteu method.²⁶ Briefly, aliquots of urine samples were thawed on ice and centrifuged for 10 minutes. The supernatant obtained was diluted 1:1 with Milli-Q water and acidified with 34 μL of hydrochloric acid (37%). In parallel, Oasis MAX plates (Waters) were prepared for (poly)phenol recovery by passing 1 mL of methanol (98%) and 1 mL of sodium acetate (50 mM, pH 7) using the extraction plate manifold for Oasis 96-Well plates (Waters, SKU: 186001831). The samples were added to the plate wells, cleaned with sodium acetate (pH 7) and 5% methanol, and finally the (poly)phenols were eluted with 2% formic acid in methanol. Fifteen microliters of the eluted samples were mixed with 170 μL of Milli-Q water, 12 μL of the Folin-Ciocalteu reagent, and 30 μL of sodium carbonate (200 g L^{-1}). The mixtures were incubated for 1 h at room temperature, protected from light. Then, 73 μL of Milli-Q water were added, and absorbance was measured at 765 nm using the same UV/Vis Multiskan spectrophotometer. Quantification was performed by comparison with a gallic acid calibration curve. For urine normalization, two methods were used. Creatinine was determined using the alkaline picrate method adapted to 96-well plates as described previously.²⁶ Three μL of the urine sample was mixed with 60 μL of picric acid solution (1%) and 5 μL of sodium hydroxide (5%). These mixtures were incubated for 15 min at room temperature in the dark. Subsequently, 232 μL of Milli-Q water were added, and absorbance was measured at 500 nm using a UV/Vis Multiskan spectrophotometer (Thermo Fisher Scientific). Creatinine concentrations were calculated using a calibration curve. In addition, we assessed urine osmolality (mOsm per kg H_2O) using freezing point depression osmometry (Gonotec Osmomat 030-D Osmometer). Total (poly)phenols were expressed as mg gallic acid equivalent (GAeq) per g creatinine. Samples were analyzed in duplicate; intra- and inter-batch coefficients of variation were below 10%.

2.6.2 Urinary individual (poly)phenol determination

2.6.2.1 Sample preparation. All urine samples were processed following the protocol of Achaintre *et al.* 2018,²⁷ with minor modifications. Samples were thawed and vortexed, and aliquots were taken for specific gravity measurement using a refractometer. Based on these values, urine samples were subsequently diluted with ultrapure water to a standardized specific gravity to normalize for urinary concentration across all samples. Then, 50 μL of each adjusted urine sample was mixed with 100 μL of Instant Buffer II and 20 μL of undiluted recombinant β -glucuronidase/arylsulfatase (Kura Biotech), followed by incubation at $52\text{ }^{\circ}\text{C}$ for 30 minutes. A pooled urine stock was also created by combining 50 μL from each gravity-adjusted sample. After incubation, 750 μL of ethyl acetate was added for protein precipitation, followed by shaking (5 min

and centrifugation (5 min, 12 000g, $4\text{ }^{\circ}\text{C}$). The supernatant was transferred to a 2 mL amber vial and evaporated to dryness under nitrogen (TurboVap, Biotage). Samples were then derivatized with 100 μL of $^{13}\text{C}_6$ -dansyl chloride (1 mg mL^{-1} in acetone) and 100 μL of carbonate buffer (pH 9.5, 0.1 M), and incubated at $60\text{ }^{\circ}\text{C}$ for 30 minutes. For pooled samples, $^{12}\text{C}_6$ -dansyl chloride was used. After derivatization, 100 μL of ACN: Milli-Q water (1:1) was added to each sample, vortexed, and transferred to a new glass vial. Quality control (QC) samples were prepared using aliquots of pooled urine; phosphate buffer solution (PBS) blanks were processed identically without urine. Each batch of 24 samples included 20 samples, two QCs (pooled urine aliquots), one blank, and one pool (pooled urine stock). Calibration standards (concentration range: 0.2–5000 ng mL^{-1}) were evaporated and derivatized identically with $^{13}\text{C}_6$ -dansyl chloride.

2.6.2.2 Sample analysis. Samples were analyzed in a single analytical sequence, consisting of two daily batches (48 samples per day). QC and blank samples were injected after every ten samples to monitor instrument performance and potential carryover. Analyses were performed using a UHPLC-MS/MS system (1290 Binary LC system, Agilent Technologies; and 4500 triple quadrupole mass spectrometer, AB Sciex). For each injection, 5 μL of the sample was mixed with 5 μL of the pooled internal standard directly in the auto-sampler before injection to the chromatographic column (Acquity UHPLC HSS T3 column, Waters). The mobile phases were A: ultrapure water/methanol (90:10, v/v) with 0.1% formic acid, and B: acetonitrile. The gradient was as follows: 0–1 min, 0% B; 1–6 min, linear increase to 50% B; 6–8.5 min, 60% B; 8.5–10.5 min, 90% B; 10.5–19 min, 100% B; 19.01–20 min, re-equilibration at 0% B. Flow rates were 0.5 mL min^{-1} (0–13 min), 0.7 mL min^{-1} (13–15 min), 1.3 mL min^{-1} (15.01–19 min), and 0.5 mL min^{-1} (19.01–20 min). Mass detection was carried out as described previously on MRM mode and using a Turbo V-ion source.²⁷ Data were acquired using Analyst® software (version 1.7.1), and quantification was carried out using SCIEX OS (version 1.6.1.29803).

Quality control was performed using data from all individually prepared QC samples. The assessment of the QC data was based on the variability of the concentration (ng mL^{-1}) from each detected compound. Relative standard deviation varied from 5 (*e.g.*, vanillic acid) to 19% (*e.g.*, equol) for 20 compounds. Values between the limit of detection (LOD) and the limit of quantification (LLOQ) were retained. For these metabolites, fewer than 10% of observations were below the LOD, and these values were imputed as $\frac{\text{LLOQ}}{\sqrt{2}}$. Eight additional compounds (apigenin, phloretin, kaempferol, isorhamnetin, resveratrol, gallic acid, gallic acid ethyl ester and quercetin) were detected in only a few samples and were, therefore, considered solely for presence/absence analyses.

2.7 Statistical analyses

Analyses were carried out using R software (version 4.4.2)²⁸ and the packages CompareGroups,²⁹ ggplot2³⁰ and FactoMineR.³¹



A statistical significance level of 95% was applied. *P*-Values were corrected for multiple comparisons using the Benjamini-Hochberg (BH) method.

Population characteristics were presented as frequencies and percentage for categorical variables and as medians and interquartile range (IQR) for continuous variables (all non-normally distributed: Shapiro-Wilk test). Differences across dietary groups were explored using the Chi-square test (Fisher's exact test for less than 5 observations) and Kruskal-Wallis (KW) test. *Post hoc* tests were applied for pairwise comparisons between diet groups (Tukey or KW with BH correction). Associations between urinary (poly)phenols and dietary (poly)phenol intakes, total (poly)phenols, the PPS, and (poly)phenol-rich food groups were evaluated using Spearman's correlation analysis.

Principal component analysis (PCA) was performed on urinary markers, applying a factor loading (FL) threshold of 0.2. Participants were subsequently classified into three clusters using *k*-means clustering based on the PCA dimensions. The selection of the optimal number of clusters was based on the silhouette and elbow methods (Fig. S1 and S2). Differences among the clusters were assessed using the KW test.

The main sources of variability in dietary and urinary (poly)phenols were evaluated using a Principal Component Partial *R*-squared (PC-PR²) analysis considering age, sex, center, BMI, profession, physical activity, smoking status, alcohol consumption, energy intake and analytical batch. Although the PC-PR² analysis showed that sociodemographic and lifestyle factors accounted for less than 1% of the overall variance in (poly)phenol intake, age and sex differed across dietary groups. Analytical batch was the only variable associated with variability in (poly)phenol markers, although its influence was negligible. These variables were therefore considered as adjustment variables in sensitivity analyses.

Adjusted geometric means of intake levels were estimated using linear regression models with log-transformed energy-adjusted intakes, further adjusting for sex and age. Likewise, urinary (poly)phenol concentrations were log-transformed and adjusted for batch (10 categories; 20 samples per batch) to obtain the adjusted concentrations.⁵ Exponentiated regression coefficients were interpreted as ratios of adjusted geometric means. In addition, linear regression models were used to evaluate the associations between ComBat batch-adjusted urinary (poly)phenols and the PPS, adjusting for analytical batch and total energy. Standardized beta coefficients (stdβ) were calculated to compare effect sizes across (poly)phenols.

Sensitivity analyses related to the dietary data were: (1) use of sex, age and batch-adjusted dietary and urinary (poly)phenol values; (2) analyses restricted to participants with a background in nutrition sciences, to provide measures of more accurate dietary intake reporting; (3) analyses restricted to participants older than 24 years or women to account for potential differences in dietary habits determined by age or sex; and (4) food contributions to total (poly)phenols calculated for a

coffee portion size of 175 mL (within the range of 150–200 mL, instead of 50 mL).

As for laboratory assessments, sensitivity analyses were: (5) excluding users of (poly)phenol-related supplements (plant extracts and other antioxidant compounds including vitamin C, vitamin D, and multivitamins); (6) testing differences in LLOQ handling: (i) excluding observations with values lower than the LLOQ and (ii) replacing values below the LLOQ (including those between the LOD and LLOQ) with $\frac{\text{LLOQ}}{\sqrt{2}}$; and (7) performing urine normalization by osmolality (GAeq/osmolality).

3. Results

3.1 Characteristics of the study population

The overall study population ($n = 792$) comprised a large proportion of women (73%), with a median age of 22 years, and generally healthy behaviors regarding alcohol consumption and smoking (Table 1). The majority were omnivores (67.4%). Among those who provided urine samples ($n = 200$; ~50% following PBDs), similar characteristics were observed for sex, age, supplement use and adherence to the hPDI (Table S5).

3.2 Food and (poly)phenol intake by diet groups

3.2.1 PB food intake. Food group consumption differences by diet groups are shown in Fig. 2A and detailed in Tables S6 and S7. Participants following PBDs reported significantly higher intakes of vegetables, whole grains, legumes, fruits, nuts, chocolate, and spices compared with omnivores ($p < 0.001$). Overall, PBD participants consumed approximately twice as many vegetables, legumes, nuts, cereals, and plant-based alternatives. Intake of coffee, tea, kombucha, and other plant-based beverages was also higher in PBD groups, particularly among vegans. Within PBD subgroups, pro-vegetarians showed the highest intakes of fresh fruits, chocolate, coffee, and tea; pesco-vegetarians of berries; and vegans of vegetables, legumes, nuts, spices, whole grains, plant-based fats, smoothies, and protein alternatives.

3.2.2 Dietary (poly)phenol intake. Intakes of (poly)phenol classes and subclasses are presented in Table 2 and Fig. 2B (*post-hoc* analyses in Table S8). Median total (poly)phenol intake was the lowest among omnivores (739.1 mg day⁻¹) and higher across all PBD groups, with vegans showing the highest intake (1120.9 mg day⁻¹). Intakes differed significantly across diet groups for most subclasses, except for flavanones and some phenolic acid subclasses (hydroxyphenylacetic and hydroxyphenylpropionic acids).

Among flavonoids, anthocyanin intake was the highest in pro-vegetarians (55.6 mg day⁻¹), followed by pesco-vegetarians (41.6 mg day⁻¹) and ovo-lacto-vegetarians (36.3 mg day⁻¹), and was the lowest in vegans and omnivores (~30 mg day⁻¹). Differences were significant between omnivores and both pesco-vegetarians ($p = 0.034$) and pro-vegetarians



Table 1 Characteristics of the OMIVECA study population ($n = 792$)

	ALL $n = 792$	OMN $n = 534$	PVG $n = 92$	PCV $n = 32$	OVL $n = 75$	VGN $n = 59$	p -Value
Sex, female	581 (73.4%)	368 (68.9%)	79 (85.9%)	31 (96.9%)	64 (85.3%)	39 (66.1%)	<0.001 ^a
Age, years	22.0 [20.0; 29.0]	21.0 [19.0; 25.0]	25.0 [21.0; 34.0]	27.0 [21.0; 36.5]	27.0 [22.0; 33.0]	32.0 [25.0; 39.5]	<0.001 ^b
BMI, kg m ⁻²	22.3 [20.4; 24.3]	22.5 [20.6; 24.5]	21.9 [20.4; 23.5]	20.4 [19.6; 22.9]	22.0 [20.5; 24.3]	21.7 [20.4; 24.1]	0.007 ^b
Center							—
Granada	576 (72.7%)	416 (77.9%)	68 (73.9%)	24 (75.0%)	45 (60.0%)	23 (39.0%)	
Madrid	70 (8.8%)	35 (6.6%)	10 (10.9%)	2 (6.2%)	13 (17.3%)	10 (16.9%)	
Seville	47 (5.9%)	25 (4.7%)	5 (5.4%)	1 (3.1%)	7 (9.3%)	9 (15.3%)	
Almería	66 (8.3%)	51 (9.6%)	8 (8.7%)	4 (12.5%)	3 (4.0%)	0 (0.0%)	
Other	33 (4.2%)	7 (1.3%)	1 (1.1%)	1 (3.1%)	7 (9.3%)	17 (28.8%)	
Profession							<0.001 ^c
Nutrition student/prof.	369 (46.6%)	273 (51.1%)	43 (46.7%)	10 (31.2%)	30 (40.0%)	13 (22.0%)	
Health sciences student/prof.	216 (27.3%)	167 (31.3%)	23 (25.0%)	11 (34.4%)	13 (17.3%)	2 (3.4%)	
Other	207 (26.1%)	94 (17.6%)	26 (28.3%)	11 (34.4%)	32 (42.7%)	44 (74.6%)	
Alcohol intake							0.031 ^c
Never	473 (59.7%)	332 (62.2%)	54 (58.7%)	12 (37.5%)	36 (48.0%)	39 (66.1%)	
Once /week	242 (30.6%)	156 (29.2%)	27 (29.3%)	17 (53.1%)	29 (38.7%)	13 (22.0%)	
≥2/week	77 (9.7%)	46 (8.6%)	11 (12.0%)	3 (9.4%)	10 (13.3%)	7 (11.9%)	
Smoking status							<0.001 ^c
Never	650 (82.1%)	458 (85.8%)	70 (76.1%)	23 (71.9%)	61 (81.3%)	38 (64.4%)	
Former	81 (10.2%)	39 (7.3%)	14 (15.2%)	7 (21.9%)	7 (9.3%)	14 (23.7%)	
Current	61 (7.7%)	37 (6.9%)	8 (8.7%)	2 (6.2%)	7 (9.3%)	7 (11.9%)	
Supplement use							<0.001 ^c
Vitamin B12	282 (35.6%)	120 (22.5%)	31 (33.7%)	12 (37.5%)	62 (82.7%)	57 (96.6%)	<0.001 ^c
Snacking	136 (17.2%)	12 (2.2%)	3 (3.3%)	5 (15.6%)	62 (82.7%)	54 (91.5%)	0.023 ^a
Yes	307 (38.8%)	210 (39.3%)	22 (23.9%)	14 (43.8%)	33 (44.0%)	28 (47.5%)	
No	485 (61.2%)	324 (60.7%)	70 (76.1%)	18 (56.2%)	42 (56.0%)	31 (52.5%)	
hPDI	56.0 [48.0; 64.0]	51.0 [46.0; 57.0]	67.0 [65.0; 70.0]	64.0 [55.0; 69.0]	67.0 [59.0; 70.5]	73.0 [68.5; 78.5]	<0.001 ^b

OMN: omnivore; PVG: pro-vegetarian; PCV: pesco-vegetarian; OVL: ovo-lacto-vegetarian; VGN: vegan; BMI: body mass index; hPDI: healthy pro-vegetarian diet index; prof.: professor. ^a n (%) for categorical variables; p -value derived from the Pearson Chi-square test. ^b Median and interquartile range for continuous variables; p -value derived from the Kruskal-Wallis test. ^c n (%) for categorical variables; p -value derived from Fisher's exact test. All p -values were corrected for multiple testing using the Benjamini-Hochberg method. Supplements – non-exclusive options: iron, vitamin B12, other B vitamins, other vitamins and minerals, yeast, and omega-3.

($p < 0.001$). A similar pattern was observed for flavanols. In contrast, flavones, flavonols, and isoflavonoids were the highest among vegans and progressively lower in the other PBD groups and omnivores. Isoflavonoid intake was nearly 100-fold higher in vegans compared with omnivores ($p < 0.001$) and showed clear differences within PBD groups (vegans: 94.8 mg day⁻¹ > ovo-lacto-vegetarians: 40.9 mg day⁻¹ > pesco-vegetarians: 17.8 > pro-vegetarians: 5.2 mg day⁻¹ > omnivores: 0.1 mg day⁻¹).

For phenolic acids, intakes of hydroxybenzoic and hydroxycinnamic acids were lower in omnivores (24.2 and 174.0 mg day⁻¹) than in PBD groups (e.g., vegans: 30.9 and 269.4 mg day⁻¹). Lignan intake also increased across dietary patterns, from 40.8 mg day⁻¹ in omnivores to 74.7 mg day⁻¹ in vegans. Stilbene intake showed only small but significant differences ($p = 0.001$).

Regarding minor subclasses, alkylphenol intake was higher in pro-vegetarians and pesco-vegetarians (>20 mg day⁻¹) than in omnivores (11.3 mg day⁻¹; $p < 0.001$). Vegans showed the highest curcuminoid intake (27.7 mg day⁻¹), significantly higher than other PBD groups (14–17 mg day⁻¹) and omnivores (2.8 mg day⁻¹). Tyrosol intake also differed across groups, with the highest intakes seen for ovo-lacto-vegetarians (37.9 mg day⁻¹) and the lowest among omnivores (27.0 mg day⁻¹; $p = 0.006$).

Fig. 2C and D display the intake profiles by (poly)phenol subclasses (flavonoids and others, respectively) across dietary patterns. Vegans exhibited pronounced peaks for isoflavonoids, flavonols, flavones, flavanones, lignans, and curcuminoids, whereas pro-vegetarians had higher peaks for chalcones, anthocyanins, flavanols, and phenolic acids. Pesco- and ovo-lacto-vegetarians displayed broadly similar profiles.

3.2.3 (Poly)phenol food sources. The contributions of food groups to total (poly)phenol intake by type of diet are presented in Fig. 2E and Tables S9 and S10. Overall, the main contributors were fresh fruits (18.2%), vegetables (14.6%), coffee and tea (12.0%), sugary items (10.6%), berries (7.9%), dark chocolate (6.9%), and nuts (5.0%).

By diet groups, among vegans, the highest contribution to (poly)phenols came from vegetables (20.8%) and fresh fruits (10.4%), whereas this pattern was reversed in omnivores and pro-vegetarians (fresh fruits > vegetables). Vegans also showed higher contributions from nuts (8.7%), legumes (3.2%), and PB protein alternatives (4.5%) and beverages (5.7%) compared with other groups ($p < 0.001$).

Pro-vegetarians had greater contributions from coffee and tea (14.7%), whole grains (2.2%), and dark chocolate (9.4%), while omnivores showed higher contributions from bakery products, potatoes, and refined cereals (4.1%, 2.2% and 1.4%).



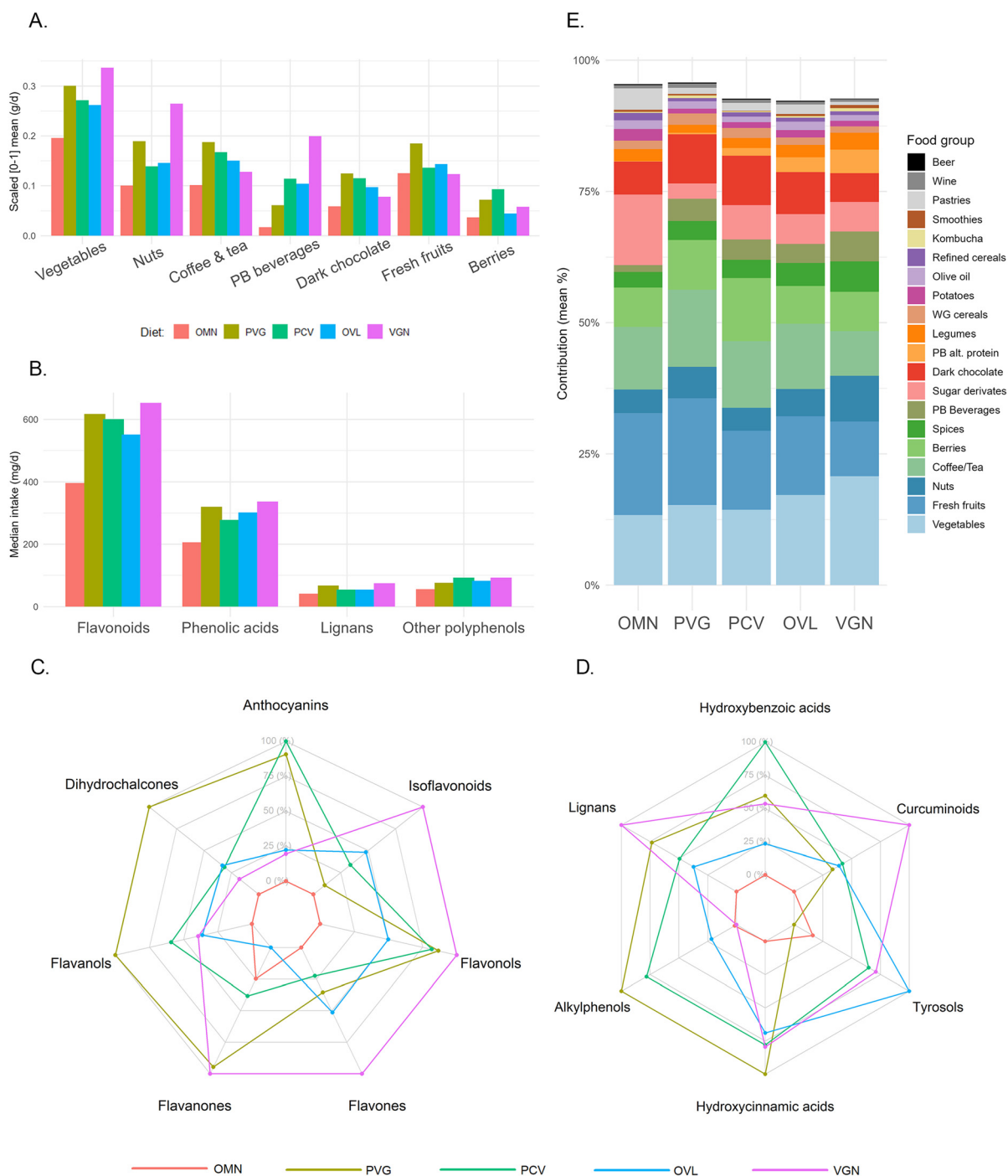


Fig. 2 Dietary (poly)phenols by type of diet and their main food contributions in the OMIVECA study sample ($n = 792$). (A) The differences by diet group of food group mean intake based on the FFQ estimations and scaled from 0 to 1, where red color represents the OMNs, olive color the PVGs, teal-green the PCV, sky blue the OVL, and magenta the VGNs. (B) The differences by diet group of the main (poly)phenol classes (median intake) with a color attribution equal to (A). (C) The contributions of the main food groups to the total (poly)phenol dietary estimation, where light blue represents the vegetables group, blue for fresh fruits, dark blue for nuts, light green for coffee and tea, green for berries, dark green for spices, brown-green for plant-based beverages, light red for sugar derivatives, red for dark chocolate, yellow-red for plant-based alternative protein, orange for legumes, brown for whole grain cereals, magenta for potatoes, light purple for olive oil, purple for refined cereals, yellow for kombucha, dark brown for smoothies, light grey for bakery and pastries, grey for wine and black for beer. The order corresponds to ascending contribution values of VGNs. (D) A radial chart showing the differences by diet group of the main flavonoid subclasses, where the scale ranges from the minimum group diet mean to the maximum group. Color attribution corresponds to the description given in (A). (E) A radial chart showing the differences by diet group of the lignan class, main phenolic acid subclasses, and tyrosols (other (poly)phenols), where the scale ranges from the minimum group diet mean to the maximum group. Color attribution corresponds to the description given in (A). Abbreviations: FFQ (food frequency questionnaire); OMN (omnivores); VGN (vegans); PCV (pesco-vegetarians); OVL (ovo-lacto-vegetarians); PVG (pro-vegetarian).





Table 2 Dietary intake of total and main (poly)phenol classes and subclasses (mg per 2000 kcal per day) by type of diet in the OMIVECA study ($n = 792$)

	ALL $n = 792$	OMN $n = 534$	PVG $n = 92$	PCV $n = 32$	OVL $n = 75$	VGN $n = 59$	p -Value
Total (poly)phenols	849.2 [634.9; 1105.5]	739.1 [569.6; 959.1]	1096.7 [880.5; 1321.1]	1089.7 [867.0; 1293.3]	988.5 [830.0; 1193.7]	1120.9 [959.4; 1442.3]	<0.001
Flavonoids	461.4 [306.9; 638.6]	396.2 [261.6; 556.6]	617.7 [451.1; 819.8]	600.9 [455.6; 721.7]	551.4 [390.8; 694.7]	653.2 [506.2; 845.1]	<0.001
Anthocyanins	32.5 [16.5; 67.1]	30.1 [15.2; 58.5]	55.6 [24.0; 100.2]	41.6 [31.4; 65.6]	36.3 [26.0; 67.8]	29.5 [11.7; 70.7]	<0.001
Dihydrochalcones	1.0 [0.4; 1.9]	0.8 [0.3; 1.8]	1.7 [0.6; 2.9]	1.2 [0.6; 1.7]	1.1 [0.4; 2.1]	0.8 [0.3; 1.8]	<0.001
Flavanols	261.0 [148.9; 400.8]	229.9 [136.8; 362.4]	383.8 [218.5; 525.7]	334.3 [232.7; 430.9]	269.0 [162.4; 415.5]	300.2 [164.4; 434.8]	<0.001
Flavanones	20.8 [9.8; 34.6]	20.2 [9.1; 33.5]	25.6 [14.7; 36.1]	21.4 [10.5; 36.8]	20.4 [13.2; 28.9]	20.1 [11.4; 36.6]	0.339
Flavones	24.9 [11.0; 46.2]	20.1 [6.4; 36.2]	31.5 [19.0; 66.3]	33.2 [21.2; 69.5]	41.7 [22.3; 94.2]	62.5 [33.7; 108.4]	<0.001
Flavonols	60.8 [41.1; 83.0]	53.4 [34.9; 70.6]	82.7 [60.3; 108.9]	79.6 [59.9; 95.3]	69.0 [57.0; 88.1]	81.3 [66.1; 122.4]	<0.001
Isoflavonoids	0.1 [0.0; 0.1]	0.1 [0.0; 0.1]	0.2 [0.0; 0.2]	0.2 [0.0; 0.2]	0.2 [0.0; 0.2]	0.2 [0.0; 0.2]	<0.001
Phenolic acids	240.8 [159.0; 350.5]	205.9 [137.1; 306.3]	320.1 [233.4; 462.4]	278.1 [231.4; 379.6]	302.2 [229.4; 366.8]	336.5 [238.7; 402.0]	<0.001
Hydroxybenzoic acids	25.6 [16.1; 45.4]	24.2 [15.0; 40.7]	28.1 [17.7; 57.1]	29.7 [25.4; 59.3]	28.3 [19.2; 45.6]	30.9 [18.5; 56.6]	<0.001
Hydroxycinnamic acids	0.6 [0.1; 1.3]	0.6 [0.1; 1.2]	0.5 [0.1; 1.0]	0.7 [0.3; 2.5]	0.7 [0.1; 2.6]	0.6 [0.4; 1.9]	0.146
Hydroxyphenylacetic acids	0.5 [0.0; 1.2]	0.5 [0.0; 1.0]	0.4 [0.0; 0.7]	0.6 [0.3; 2.2]	0.60 [0.0; 2.3]	0.5 [0.3; 1.6]	0.220
Hydroxyphenylpropanoic acids	47.1 [33.1; 64.9]	40.8 [29.0; 55.4]	67.2 [50.0; 91.1]	54.0 [44.3; 67.9]	53.9 [40.4; 65.9]	74.7 [51.9; 97.6]	<0.001
Lignans	0.2 [0.1; 0.4]	0.2 [0.1; 0.4]	0.2 [0.1; 0.4]	0.3 [0.1; 0.4]	0.2 [0.1; 0.4]	0.1 [0.0; 0.3]	0.001
Stilbenes	64.2 [41.5; 95.8]	55.1 [37.2; 86.2]	75.9 [54.6; 99.3]	92.7 [67.1; 126.6]	82.6 [55.5; 127.4]	92.9 [70.5; 128.0]	<0.001
Other (poly)phenols	0.4 [0.1; 0.9]	0.4 [0.1; 0.7]	0.7 [0.1; 1.2]	0.4 [0.2; 0.9]	0.5 [0.1; 1.1]	0.3 [0.1; 0.8]	<0.001
Alkylmethoxyphenols	13.3 [4.0; 25.2]	11.3 [3.1; 23.0]	22.0 [13.3; 29.9]	20.3 [7.9; 26.2]	15.8 [5.8; 26.0]	13.2 [4.2; 23.8]	<0.001
Alkylphenols	4.9 [1.5; 20.1]	2.8 [0.0; 13.3]	14.4 [3.8; 25.9]	16.2 [6.0; 29.4]	17.1 [5.1; 25.5]	27.7 [14.1; 60.8]	<0.001
Curcuminoids	0.2 [0.1; 0.3]	0.2 [0.1; 0.3]	0.3 [0.2; 0.4]	0.2 [0.1; 0.4]	0.3 [0.2; 0.4]	0.3 [0.2; 0.6]	<0.001
Furanocoumarins	29.1 [17.0; 50.9]	27.0 [15.2; 47.1]	29.2 [19.4; 42.7]	34.4 [20.0; 78.7]	37.9 [20.9; 87.8]	36.0 [24.0; 64.4]	0.001
Tyrosols	0.7 [0.4; 1.3]	0.7 [0.4; 1.3]	0.9 [0.3; 1.2]	0.8 [0.5; 1.1]	1.0 [0.4; 1.4]	0.6 [0.2; 1.1]	0.481
Other (unclassified)							

Median and interquartile range; p -value derived from the Kruskal–Wallis test. All p -values were corrected for multiple testing using the Benjamini–Hochberg method. (Poly)phenols were classified into major classes and subclasses according to the Phenol-Explorer classification, with alkylphenols, curcuminoids, furanocoumarins, and tyrosols grouped under the ‘other (poly)phenols’ category. Chalcones, dihydroflavonols, hydroxybenzaldehydes, hydroxybenzoketones, hydroxybenzofuranones, hydroxycoumarins, hydroxyphenylpropanes, methoxyphenols, and naphthoquinones are not presented due to the low values for all the groups. OMN: omnivore; PVG: pro-vegetarian; PCV: pesco-vegetarian; OVL: ovo-lacto-vegetarian; VGN: vegan.

The contribution of sugary items, predominantly from bottled fruit juices, was 13.4%, more than twice that observed in PBD groups ($p < 0.001$). Contributions from berries, alcoholic beverages, and smoothies did not differ significantly across groups.

3.3 Urinary (poly)phenols

3.3.1 Total urinary (poly)phenols and urinary metabolites.

Total urinary (poly)phenol concentrations were higher in all PBD groups than in omnivores (e.g., vegans: 215.0 vs. omnivores: 132.1 mg gallic acid equivalents per g creatinine). No significant differences were observed among PBD groups, whereas all differed significantly from omnivores ($p < 0.001$; Table S11).

Geometric means of the urinary (poly)phenol levels adjusted for batch are shown in Table 3 and *post-hoc* p -values in Table S12. No differences were observed for urinary equol and 3-hydroxyphenylacetic acid concentrations across the five diet groups. For all the other biomarkers, omnivores showed lower levels than PBD groups. Overall, vegans had the highest mean urinary (poly)phenol concentrations, particularly compared with omnivores. Elevated urinary levels in vegans were observed for several phenolic acids (e.g., protocatechuic acid: 4.4, ferulic acid: 31.4, and *p*-coumaric acid: 6.7 ng mL⁻¹); flavonoids (naringenin: 108.3 and hesperetin: 29.9 ng mL⁻¹), isoflavonoids (genistein: 469.0 and daidzein: 746.9 ng mL⁻¹), and lignans (enterolactone: 175.9 and enterodiol: 115.2 ng mL⁻¹). Differences among PBD groups were most pronounced for genistein, daidzein, and enterodiol, with the highest values in vegans. Pro-vegetarians and pesco-vegetarians showed broadly similar profiles. Notably, pro-vegetarians showed the highest hesperetin, hydroxytyrosol and tyrosol concentrations (31.7, 41.4, and 23.4 ng mL⁻¹, respectively). Unadjusted urinary individual (poly)phenol levels are shown in Fig. 3A and Table S11 (*post-hoc* analyses in Table S13).

Data of compounds with >10% values below the LOD are shown in Table S14. When considering only detectable values, differences were observed for apigenin and kaempferol, with lower prevalence of apigenin and higher prevalence of kaempferol among vegans.

3.3.2 Urinary (poly)phenols PCA. PCA of urinary (poly)phenols identified three principal components explaining 36.9% of the total variance (Table S15). The first component featured mainly tyrosols (FL > 0.7) and several phenolic acids, whereas the second component was characterized by isoflavonoids (genistein, daidzein, and equol: FL > 0.6), among others. The third component showed negative loadings for hesperetin, naringenin, and *m*- and *p*-coumaric acids (FL < -0.6).

k-Means clustering revealed three clusters with distinct urinary profiles (Tables S16 and S17). Cluster 1 included exclusively PBD followers, mostly vegans, and showed high levels of isoflavonoid-related markers (genistein: > 1000 ng mL⁻¹). Cluster 2 comprised predominantly PBD participants (>70%) and was characterized by higher levels of ty-

rosols and phenolic acids, and intermediate levels of enterolactone and enterodiol. Cluster 3 consisted mainly of omnivores (68.6%) and showed overall lower urinary (poly)phenol concentrations compared with the other clusters ($p < 0.001$).

3.3.3 Urinary (poly)phenols and food and (poly)phenols intake correlations. Spearman's correlation coefficients between dietary (poly)phenol intake and urinary (poly)phenol concentrations are presented in Fig. 3B, and in Fig. S3, where correlation with (poly)phenol-rich food sources is also shown. Dietary intakes corresponding to these urinary biomarkers are detailed in Tables S18 and S19.

The strongest correlations were observed for the isoflavonoids genistein and daidzein, which were highly inter-correlated in both dietary and urinary data ($\rho > 0.60$) and also correlated with the total isoflavonoid intake ($\rho = 0.63$ and 0.60). Dietary intake of these compounds was markedly higher among vegans (>3 mg per 2000 kcal) than among omnivores (<0.1 mg per 2000 kcal; $p < 0.001$).

Weak-to-moderate correlations ($\rho = 0.2$ – 0.3) between urinary biomarkers and their dietary counterparts were also found for hesperetin, naringenin, hydroxytyrosol, tyrosol, and homovanillic acid. While enterodiol and enterolactone are microbiota-derived metabolites, their urinary levels showed low-to-moderate correlations with lignan precursors (matairesinol: $\rho \sim 0.30$) and total dietary lignans ($\rho \sim 0.25$). Urinary total (poly)phenols were also weak-to-moderately correlated with several urinary metabolites (Fig. 3C), most notably ferulic acid, *p*-coumaric acid, vanillic acid, enterodiol, enterolactone, caffeic acid, and genistein.

Consumption of key foods rich in (poly)phenols was correlated with some urinary markers (Fig. S3), namely: tofu, soy milk beverage and PB alternative proteins (soy-derived products) with daidzein and genistein ($\rho > 0.51$), seeds and whole grain cereals with enterolactone and enterodiol ($\rho > 0.25$), oranges with naringenin and hesperetin ($\rho = 0.25$), coffee with caffeic acid ($\rho = 0.23$), and some vegetables such as onion, cabbage and broccoli with hydroxycinnamic acids such as *m*- and *p*-coumaric, and ferulic acids ($\rho > 0.23$). Other weak associations (e.g., olives and equol) likely reflected the overall dietary patterns rather than direct food sources.

3.4 (Poly)phenol diet score

The PPS was higher in PBD groups than in omnivores ($p < 0.001$). No significant differences were observed among PBD subgroups (Table S20). Total urinary (poly)phenols correlated with the PPS ($\rho = 0.37$). Furthermore, the PPS was strongly correlated with total dietary (poly)phenol intake ($\rho = 0.55$) and with the hPDI ($\rho = 0.62$).

Table 4 shows effect sizes resulting from the association between the urinary (poly)phenols and the PPS. Batch-adjusted models showed significant associations with the metabolites, except equol and 3-hydroxybenzoic acid. The std β values varied





Table 3 Geometric means (ng mL⁻¹) and effect sizes of urinary polyphenols adjusted for batch in the urine sample study population (*n* = 200)

Urine metabolite	OMN	PVG	PCV	OVL	VGN	<i>p</i> -Value	OMN-PVG	OMN-PCV	OMN-OVL	OMN-VGN	PVG-PCV	PVG-OVL	PVG-VGN	PCV-OVL	PCV-VGN	OVL-VGN
Naringenin	15.2	47.1	19.0	29.7	108.3	<0.001	0.32 [0.11; 0.97]	0.80 [0.24; 2.62]	0.51 [0.23; 1.13]	0.14 [0.05; 0.40]	2.48 [0.57; 10.82]	1.58 [0.49; 5.15]	0.43 [0.11; 1.68]	0.64 [0.18; 2.29]	0.18 [0.04; 0.72]	0.27 [0.09; 0.86]
Hesperetin	4.4	31.7	8.3	4.2	27.9	<0.001	0.14 [0.02; 0.81]	0.53 [0.08; 3.56]	1.05 [0.29; 3.71]	0.16 [0.03; 0.86]	3.80 [0.36; 40.15]	7.47 [1.13; 49.46]	1.14 [0.13; 9.89]	1.97 [0.25; 15.20]	0.30 [0.03; 2.90]	0.15 [0.02; 0.94]
Daidzein	3.9	15.6	22.2	76.0	746.9	<0.001	0.25 [0.05; 1.28]	0.18 [0.03; 1.02]	0.05 [0.02; 0.17]	0.01 [0.00; 0.02]	0.70 [0.08; 6.15]	0.21 [0.04; 1.17]	0.02 [0.00; 0.15]	0.29 [0.04; 1.92]	0.03 [0.00; 0.24]	0.10 [0.02; 0.54]
Genistein	4.6	13.5	23.8	75.4	469.0	<0.001	0.34 [0.07; 1.58]	0.19 [0.04; 1.01]	0.06 [0.02; 0.18]	0.01 [0.00; 0.04]	0.57 [0.07; 4.47]	0.18 [0.03; 0.94]	0.03 [0.00; 0.19]	0.32 [0.05; 1.89]	0.05 [0.01; 0.37]	0.16 [0.03; 0.79]
Equol	1.9	5.0	3.5	4.2	4.3	0.066	0.38 [0.09; 1.67]	0.54 [0.11; 2.67]	0.46 [0.11; 1.32]	0.44 [0.11; 1.80]	1.42 [0.20; 10.19]	1.20 [0.25; 5.81]	1.15 [0.19; 7.02]	0.84 [0.15; 4.66]	0.81 [0.12; 5.42]	0.96 [0.21; 4.40]
Enterolactone	55.8	91.2	99.6	104.0	175.9	0.025	0.61 [0.18; 2.05]	0.56 [0.15; 2.06]	0.54 [0.23; 1.28]	0.32 [0.10; 1.00]	0.92 [0.18; 4.60]	0.88 [0.24; 3.20]	0.52 [0.12; 2.28]	0.96 [0.24; 3.89]	0.57 [0.12; 2.68]	0.59 [0.17; 2.05]
Enterodiol	16.4	28.0	29.7	33.7	115.2	<0.001	0.59 [0.18; 1.88]	0.55 [0.16; 1.94]	0.49 [0.21; 1.13]	0.14 [0.05; 0.43]	0.94 [0.20; 4.46]	0.83 [0.24; 2.89]	0.24 [0.06; 1.01]	0.88 [0.23; 3.39]	0.26 [0.06; 1.15]	0.29 [0.09; 0.97]
Hydroxytyrosol	17.6	41.4	30.1	22.7	26.6	<0.001	0.42 [0.23; 0.77]	0.58 [0.31; 1.11]	0.78 [0.51; 1.19]	0.66 [0.38; 1.16]	1.38 [0.62; 3.04]	1.83 [0.97; 3.45]	1.56 [0.75; 3.22]	1.33 [0.67; 2.64]	1.13 [0.53; 2.43]	0.85 [0.46; 1.57]
Tyrosol	13.5	23.4	15.6	16.0	16.3	0.003	0.58 [0.38; 0.88]	0.87 [0.55; 1.37]	0.84 [0.62; 1.14]	0.83 [0.55; 1.24]	1.50 [0.85; 2.65]	1.46 [0.92; 2.30]	1.44 [0.85; 2.42]	0.97 [0.59; 1.59]	0.96 [0.55; 1.66]	0.98 [0.63; 1.53]
Protocatechuic acid	1.4	2.0	2.4	2.9	4.4	<0.001	0.67 [0.37; 1.23]	0.57 [0.30; 1.09]	0.47 [0.31; 0.72]	0.31 [0.18; 0.56]	0.85 [0.38; 1.88]	0.70 [0.37; 1.33]	0.47 [0.22; 0.97]	0.83 [0.41; 1.65]	0.55 [0.25; 1.19]	0.67 [0.36; 1.24]
3,4-Dihydroxyphenylacetic acid	0.8	1.6	1.5	2.2	1.8	<0.001	0.49 [0.24; 0.98]	0.51 [0.24; 1.09]	0.34 [0.21; 0.57]	0.42 [0.21; 0.82]	1.05 [0.41; 2.69]	0.71 [0.33; 1.51]	0.86 [0.36; 2.04]	0.68 [0.30; 1.54]	0.82 [0.33; 2.04]	1.21 [0.59; 2.51]
4-Hydroxybenzoic acid	8.7	10.7	12.8	12.8	15.6	<0.001	0.81 [0.51; 1.30]	0.68 [0.41; 1.14]	0.68 [0.48; 0.96]	0.56 [0.35; 0.88]	0.84 [0.45; 1.58]	0.84 [0.50; 1.39]	0.84 [0.38; 1.23]	1.00 [0.58; 1.73]	0.82 [0.44; 1.51]	1.25 [0.72; 2.16]
3-Hydroxybenzoic acid	0.4	0.5	0.7	0.6	0.5	0.015	0.82 [0.50; 1.34]	0.80 [0.47; 1.36]	0.57 [0.32; 1.01]	0.66 [0.45; 0.97]	0.83 [0.50; 1.37]	0.71 [0.35; 1.45]	0.82 [0.47; 1.46]	1.03 [0.54; 1.98]	1.16 [0.62; 2.14]	1.44 [0.73; 2.86]
3-Hydroxyphenylacetic acid	65.2	55.7	86.1	79.3	84.9	0.120	1.17 [0.67; 2.04]	0.76 [0.42; 1.38]	0.82 [0.55; 1.22]	0.77 [0.45; 1.30]	0.65 [0.31; 1.36]	0.70 [0.39; 1.27]	0.66 [0.33; 1.29]	1.09 [0.57; 2.07]	1.01 [0.50; 2.07]	0.93 [0.53; 1.65]
<i>m</i> -Coumaric acid	1.3	3.3	2.6	4.8	4.1	<0.001	0.40 [0.15; 1.07]	0.51 [0.18; 1.46]	0.28 [0.14; 0.56]	0.33 [0.13; 0.84]	1.26 [0.34; 4.67]	0.69 [0.24; 1.96]	0.82 [0.25; 2.71]	0.54 [0.17; 1.69]	0.65 [0.18; 2.28]	1.19 [0.43; 3.26]
<i>p</i> -Coumaric acid	3.9	4.7	5.2	6.2	6.7	<0.001	0.82 [0.53; 1.26]	0.74 [0.47; 1.18]	0.62 [0.46; 0.85]	0.58 [0.38; 0.87]	0.91 [0.51; 1.61]	0.76 [0.48; 1.20]	0.70 [0.42; 1.19]	0.84 [0.51; 1.38]	0.78 [0.45; 1.35]	0.93 [0.60; 1.45]
Vanillic acid	12.9	20.6	24.6	29.0	33.5	<0.001	0.62 [0.35; 1.11]	0.52 [0.28; 0.97]	0.44 [0.29; 0.67]	0.38 [0.22; 0.66]	0.84 [0.39; 1.80]	0.71 [0.38; 1.31]	0.62 [0.30; 1.25]	0.85 [0.44; 1.65]	0.74 [0.35; 1.54]	0.87 [0.48; 1.57]
Homovanillic acid	9.6	10.5	15.0	13.8	12.5	<0.001	0.91 [0.65; 1.27]	0.64 [0.45; 0.91]	0.70 [0.55; 0.89]	0.77 [0.56; 1.06]	0.70 [0.45; 1.09]	0.77 [0.54; 1.09]	0.84 [0.56; 1.27]	1.09 [0.74; 1.60]	1.20 [0.78; 1.84]	1.10 [0.78; 1.55]
Ferulic acid	17.3	21.3	21.2	31.2	31.4	<0.001	0.34 [0.07; 1.58]	0.19 [0.04; 1.01]	0.06 [0.02; 0.18]	0.01 [0.00; 0.04]	0.57 [0.07; 4.47]	0.18 [0.03; 0.94]	0.03 [0.00; 0.19]	0.32 [0.05; 1.89]	0.05 [0.01; 0.37]	0.16 [0.03; 0.79]
Caffeic acid	3.4	4.5	5.4	6.6	7.0	<0.001	0.32 [0.11; 0.97]	0.80 [0.24; 2.62]	0.51 [0.23; 1.13]	0.14 [0.05; 0.40]	2.48 [0.57; 10.82]	1.58 [0.49; 5.15]	0.43 [0.11; 1.68]	0.64 [0.18; 2.29]	0.18 [0.04; 0.72]	0.27 [0.09; 0.86]

Geometric means (energy-adjusted to 2000 kcal) of urinary metabolites were estimated from linear models and adjusted for age, sex, and batch. Effect sizes are expressed as ratios of geometric means (GMR) for pairwise comparisons between diet groups; 95% confidence intervals (CI) are presented in brackets. Global *p*-values were obtained from the overall model (ANOVA), and pairwise comparisons were performed using Tukey's method to account for multiple testing. Abbreviations: OMN, omnivore; PVG, pro-vegetarian; PCV, pesco-vegetarian; OVL, ovo-lacto-vegetarian; VGN, vegan.

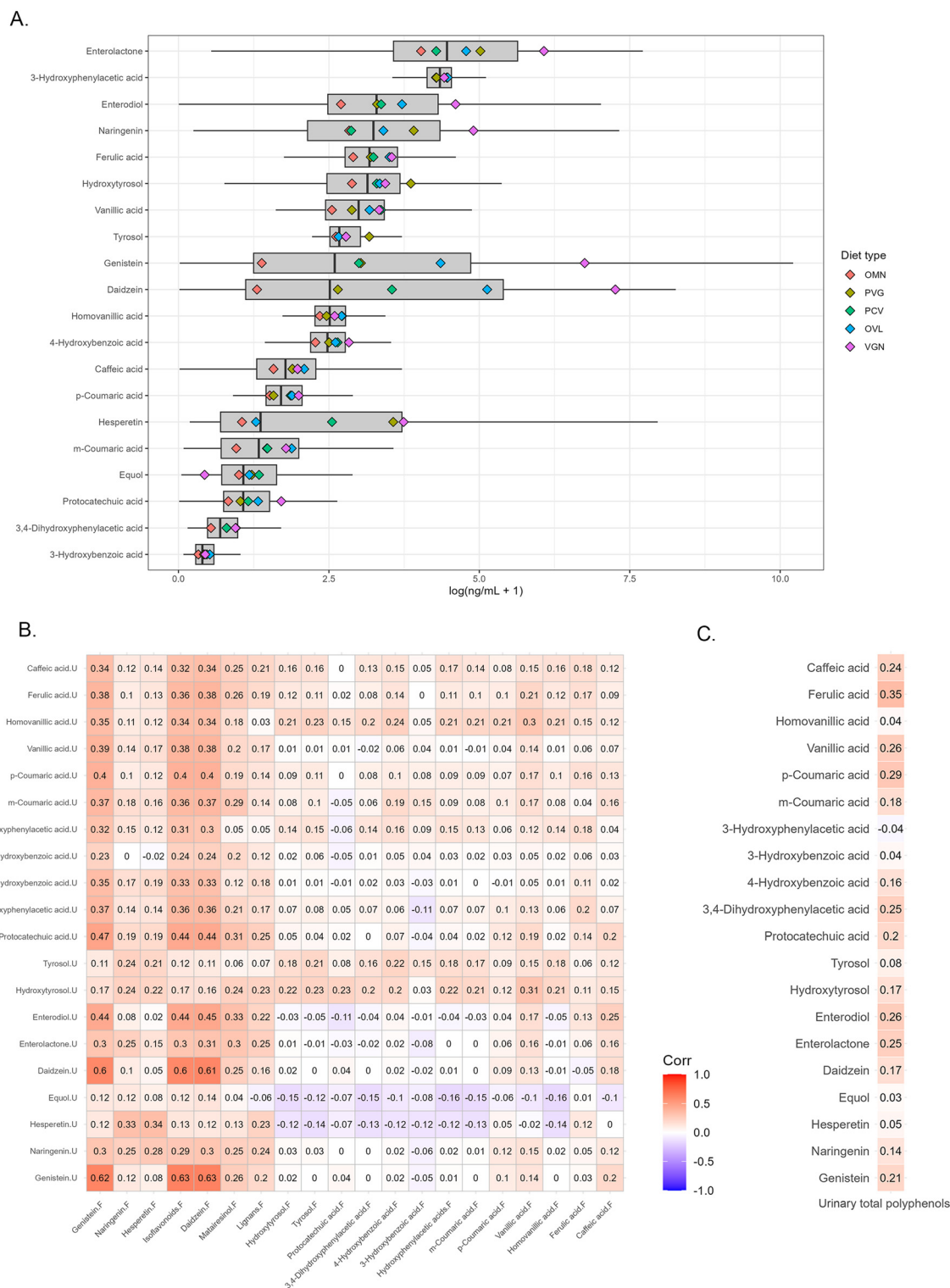


Fig. 3 Urine (poly)phenol boxplots and correlations between the urinary (U) and dietary (F) (poly)phenols in the urine sample study population ($n = 200$). (A) Boxplot shows the minimum, maximum, and quartile intervals of each metabolite. Rhombus symbols correspond to diet group medians with the color attribution being: red color for OMNs, olive color for PVG, teal-green for PCV, sky blue for OVL, and magenta for VGNs. (B) Correlogram of FFQ-derived (poly)phenols and urine (poly)phenols, showing the Spearman correlation coefficients between urine metabolites (in rows, and denoted as "U") and the dietary intake of the same (poly)phenol (in columns, and denoted as "F"). (C) Correlation diagram showing the Spearman correlation coefficients of each urine metabolite to urinary total (poly)phenols measured using the Folin-Ciocalteu method. Positive correlations are indicated in red and the negative ones are indicated in blue. Abbreviations: FFQ (food frequency questionnaire); OMN (omnivores); VGN (vegans); PCV (pesco-vegetarians); OVL (ovo-lacto-vegetarians); PVG (pro-vegetarian).



Table 4 Effect sizes for associations between urinary (poly)phenols and the PPS in the urine subsample population ($n = 200$)

Urinary (poly)phenols	R^2	std β	SE	p -Value	Corrected p -value
Urinary total (poly)phenols	0.102	0.320	0.068	<0.001	<0.001
Ferulic acid	0.097	0.310	0.068	<0.001	<0.001
<i>p</i> -Coumaric acid	0.096	0.301	0.068	<0.001	<0.001
Protocatechuic acid	0.091	0.294	0.068	<0.001	<0.001
Caffeic acid	0.094	0.284	0.068	<0.001	<0.001
Vanillic acid	0.080	0.280	0.069	<0.001	<0.001
<i>m</i> -Coumaric acid	0.077	0.269	0.069	<0.001	<0.001
Enterodiol	0.067	0.258	0.069	<0.001	0.001
Genistein	0.079	0.248	0.069	<0.001	0.001
Tyrosol	0.060	0.240	0.069	0.001	0.001
Naringenin	0.057	0.230	0.069	0.001	0.002
Daidzein	0.061	0.232	0.069	0.001	0.002
Hydroxytyrosol	0.054	0.226	0.070	0.001	0.002
4-Hydroxybenzoic acid	0.048	0.219	0.070	0.002	0.003
Enterolactone	0.047	0.214	0.070	0.002	0.003
3-Hydroxyphenylacetic acid	0.039	0.195	0.070	0.006	0.008
3,4-Dihydroxyphenylacetic acid	0.059	0.177	0.069	0.011	0.014
Homovanillic acid	0.040	0.175	0.070	0.014	0.016
Hesperetin	0.023	0.148	0.071	0.038	0.042
Equol	0.020	0.132	0.071	0.063	0.063
3-Hydroxybenzoic acid	0.018	0.133	0.071	0.062	0.063

Standardized betas (std β) derived from linear regression models assessing effect sizes of batch-adjusted urinary (poly)phenols and PPS. SE: standard error. R^2 : explained variance. All p -values were corrected for multiple testing using the Benjamini–Hochberg method. Total urinary (poly)phenols are corrected for creatinine excretion levels.

from moderate effects sizes (~ 0.3 ; *e.g.*, ferulic and *p*-coumaric acids) to smaller effects (~ 0.1 ; *e.g.*, homovanillic acid and hesperetin). For total urinary (poly)phenols, a 1-SD increase in PPS was associated with a 0.32-SD increase in urinary concentrations.

3.5 Sensitivity analyses

Differences in urinary (poly)phenol concentrations by lifestyle variables (PC-PR²) were only manifested (1%) for few compounds: 3,4-dihydroxyphenylacetic and homovanillic acids by sex, tyrosol by smoking status, and caffeic acid by total energy intake (data not shown). Concerning dietary sensitivity analyses, adjusted analyses yielded similar trends, including subclass intakes (per 2000 kcal day⁻¹) adjusted for age and sex (Table S21) and energy-unadjusted (poly)phenol intakes (Table S22). Analyses restricted to females (Table S23), participants older than 24 years (Table S24), and those in nutrition-related fields (Table S25) produced consistent results. Also, coffee and tea were the main contributors to total (poly)phenols when a coffee portion size of 150–200 mL was considered (Table S26), this being true for all diet types (25.5% in omnivores, 30.7% in pro-vegetarians, and around 27% in vegetarians/vegans).

In laboratory assessment sensitivity analyses, excluding participants reporting (poly)phenol-related supplement intake (Table S27) and applying alternative approaches to handle values below the LLOQ yielded results consistent with the main analyses (Tables S28 and S29). Similarly, normalization of total (poly)phenols based on osmolality led to similar results (data not shown).

4. Discussion

This study provides the first comprehensive characterization of (poly)phenol exposure across different PDBs, including vegan, ovo-lacto-, pesco-, pro-vegetarian, and conventional omnivorous diets, integrating both dietary intakes and urinary concentrations of these compounds. PDBs are characterized by higher total (poly)phenol intake and distinct (poly)phenol subclasses—such as anthocyanins, flavanols, flavones, flavonols, flavonoids, phenolic acids, tyrosols, and lignans—compared to a non-PBD. These differences in intake profiles are driven by vegetables, fruits, whole grains, coffee, nuts, cocoa/chocolate, spices, soy and soy-derived products, and legumes, resulting in distinct dietary and urinary (poly)phenol profiles. These patterns differed not only between omnivores and the PBD groups, but also among PDBs themselves, reflecting variations in their main food sources (*e.g.*, higher contributions of vegetables and soy-derived products to (poly)phenol intake among vegans). Vegans and pesco-vegetarians showed the highest intake levels of most dietary (poly)phenols. Dietary (poly)phenol intake correlated with only a few urinary (poly)phenols, mainly daidzein and genistein, supporting their link with absorption, metabolism, and excretion, and endorsing their use as objective biomarkers of (poly)phenol intake in nutritional studies. This relationship also supports, in part, the validity of the FFQ used in this study to assess PDBs and (poly)phenol intake.

Previous studies on the characterization of dietary (poly)phenol intake in PDBs have also observed significant differences depending on the dietary pattern. In the study of Adventists in the US, involving 77 441 participants (mean age



57 years), an average total (poly)phenol intake of 801 mg day⁻¹ was reported.¹⁶ This study used a 204-item FFQ and applied the USDA and Phenol-Explorer databases to estimate (poly)phenol intake. Surprisingly, higher (poly)phenol intakes were reported in omnivores (662 mg day⁻¹) than in vegans (498 mg day⁻¹) in this study, a finding that contradicts our results. In the OMIVECA study, total (poly)phenol intake was higher in PBDs (>1000 mg per day per 2000 kcal) than in omnivores (~750 mg day⁻¹), supporting that PBDs provide greater amounts of dietary (poly)phenols than non-PBDs. These discrepancies between studies may be partly explained by the contribution of coffee to the (poly)phenol intake. In the Adventist study, coffee accounted for 65% of total intake, and no differences between dietary groups were observed among non-coffee drinkers. By contrast, the contribution of coffee-derived (poly)phenols in our study was substantially lower (12%). The reason behind this could be the portion size of coffee and tea considered in our study, which was set at 50 mL for both (standard Spanish serving size).²⁰ While the FFQ used in OMIVECA included the portion size in mL along with the specification of “1 cup”, this item may have been misreported by the participants, since 1 cup may correspond to larger volumes. Indeed, other studies used larger portion sizes (190 mL).⁹ If a larger coffee portion size (e.g., 175 mL) is considered, overall, the estimated contribution of coffee to total dietary (poly)phenols is approximately 30%. Differences with the Adventist study may be also explained by the dietary habits captured in OMIVECA reflecting a more Mediterranean-oriented dietary pattern. Other reasons may be related to methodological issues, including the (poly)phenol databases used and a more comprehensive assessment of (poly)phenol-rich foods. In OMIVECA, foods such as chocolate, spices, PB beverages, and other novel plant-based products available on the market were considered.

In our study, fruits, chocolate, and vegetables accounted for 48.5% of total (poly)phenol intake. The consumption of these foods led to significant differences between the diet groups across several (poly)phenol subclasses: anthocyanins (mainly driven by higher fruit intake in PBDs), curcuminoids (possibly due to the greater use of spices to enhance flavor in PBDs), flavones (associated with green leafy vegetables), flavonols (such as quercetin, primarily from vegetables like onions and broccoli), isoflavonoids (linked to soy and soy-derived product consumption in PBDs), and lignans (related to higher intakes of whole grains, fruits, and vegetables in PBDs). These differences in the (poly)phenol intake may have relevant health implications. In fact, the potential health benefits of PBDs in relation to chronic diseases including diabetes, cancer and cardiovascular diseases, may be partly attributed to the higher abundance of (poly)phenols in these dietary patterns.^{32,33}

The other study on (poly)phenol intake in PBDs is the EPIC study.³ This study considered 309 vegans and vegetarians (the “UK health-conscious group”) from the EPIC-Oxford cohort (age range: 35–74 years). Information on (poly)phenol intake was derived from a single 24 hour dietary recall and through Phenol-Explorer. Across the 10 participating countries, (poly)phenol intake ranged from 584 to 1786 mg day⁻¹, with the veg-

etarian cohort showing one of the highest intakes (1521 mg day⁻¹), particularly flavonoids and lignans. These findings are broadly consistent with those observed in the OMIVECA study. The EPIC-Oxford cohort also reported higher consumption of soy, legumes, nuts, fruits, and vegetables among vegetarians, whereas omnivorous diets were richer in vegetables, fruits, legumes, and nuts.³³ Similarly to our findings, the intake of vegetables, fruits, and other plant-based foods was higher in vegetarian and vegan diets. However, we could not confirm the contribution of wine to (poly)phenol intake across diet groups due to the low level of consumption in OMIVECA.

A systematic review on methods to estimate dietary (poly)phenol intake reported that most studies relied on FFQs ($n = 449$ studies; 73%), while only 35% used Phenol-Explorer and/or USDA food composition tables, and few applied biomarkers of intake (7%).⁴ FFQs varied widely in the number of items and often omitted key flavonoid-rich foods (e.g., soy products), limiting comparability across studies. Twenty-four-hour dietary recalls of more than two days or diet records were used in 5% of the studies only, despite being considered the most suitable methods to estimate dietary (poly)phenol intake; they are less prone to bias and allow a more accurate food assignment to the Phenol-Explorer/USDA database.⁴ Consequently, the review concluded that FFQs could be more feasible tools for assessing long-term (poly)phenol intake in large population studies.⁴ In this context, specific (poly)phenol FFQs have recently been developed, such as the KP-FFQ in the UK, whose validation study supports that this tool could estimate (poly)phenol intake.³⁴ Our study, using an adapted Spanish FFQ together with urinary (poly)phenol markers, supports the feasibility of estimating dietary (poly)phenol intake with this tool. By integrating dietary assessment methods with nutritional biomarkers, our results provide more reliable estimates, in line with current recommendations to combine dietary tools with biomarkers to improve validity and reduce measurement error.^{9,35}

In our study, positive correlations were observed between dietary daidzein and genistein intake, consumption of legumes and soy-derived products, and the excreted levels of these compounds. This finding is highly relevant as it supports the validity of these isoflavones as objective markers of soy and legume intake. Consistent with our results, a separate analysis within the EPIC study also reported associations between dietary intake and urinary excretion of soy-related compounds. Specifically, this EPIC analysis showed that vegetarian diets, characterized by higher consumption of soy and legumes, were associated with significantly higher urinary levels of genistein, daidzein, and equol compared with omnivorous diets.¹⁷ In that study, (poly)phenol intake estimates were based on 24 hour dietary recalls and 24 hour urine collections, and the USDA and Phenol-Explorer databases.¹⁷ Moreover, these markers enabled the identification of a PB dietary cluster using PCA. To the best of our knowledge, no previous study has examined such clusters in the context of PBDs. Urine samples were collected from the first morning void to obtain a more representative and less diluted concen-



tration of (poly)phenols, thereby enabling a more accurate assessment of their excretion and bioavailability after intake.³⁶ Another consideration is that, when it comes to PBDs, urinary biomarkers may be biased by creatinine excretion due to the avoidance or restriction of animal-based foods.³⁷ This issue may have affected our results; however, sensitivity analyses based on osmolality normalization suggested that the main findings were robust.

The bioavailability of flavonoids is a key determinant of their suitability as nutritional biomarkers. Many flavonoids exhibit limited absorption, extensive metabolism, and rapid elimination, making their detection in biological samples challenging.^{7,36} Therefore, sensitive analytical techniques such as LC-MS/MS are required to identify and quantify metabolites at very low concentrations. Nevertheless, even with such techniques, certain compounds, such as apigenin, may remain difficult to detect due to their low concentrations and predominance as conjugated forms.^{8,38} This may have limited their detection in our study. This should be interpreted with caution as not all phenolic compounds were affected. For instance, compounds such as daidzein and genistein showed a more favorable profile due to their greater specificity, stability in biological samples, and lower inter-individual variability. These compounds, mainly absorbed as glycosides (genistin and daidzin), are being considered robust biomarkers of soy and legume intake.^{5,8,39} In line with this, our study confirmed higher consumption of soy-derived foods in PBDs, including PB beverages and meat alternatives, and higher urinary levels of these isoflavones. Isoflavones have been associated with protective effects against several chronic diseases,⁴⁰ which may also partly explain the health benefits of PBDs. Notably, we observed high isoflavone intake in the vegan group, with a median of ~ 3 mg day⁻¹ of genistein and daidzein. This level falls within the potentially beneficial range reported in a recent US cohort study, where intakes of 3.34 mg day⁻¹ genistein and 2.47 mg day⁻¹ daidzein were associated with reduced all-cause and cardiovascular mortality.⁴¹

In our study, significant differences were also found between PBDs and omnivores concerning dietary and/or urinary (poly)phenols, including naringenin, tyrosol and hydroxytyrosol, and multiple phenolic acids including protocatechuic acid, *m*- and *p*-coumaric acid, vanillic acid, homovanillic acid, ferulic acid, and caffeic acid, among others. Our study, however, did not detect significant differences in equol levels across dietary groups. Equol is a microbiota-derived metabolite of daidzein, and its production depends on individual gut microbiota composition and the capacity to generate this compound. Only a subset of individuals are therefore “equol producers”,^{42,43} which may explain the lack of consistent variation across the diet groups in our study. This finding further suggests that equol is neither a direct marker of dietary (poly)phenol intake, nor valid to discriminate between PBDs. In contrast, enterodiol—a urinary metabolite produced from lignans in fiber-rich plant foods—was higher among vegans (and PBDs overall), in line with their greater lignan intake.

Similar findings have been reported in other populations, where higher enterolignan levels were associated with increased consumption of vegetables and soy products.^{44,45} Hydroxytyrosol, a bioactive compound from olives and olive oil with established cardioprotective properties,⁴⁶ was also higher in PBDs, with the pro-vegetarian group showing nearly double the urinary levels observed in omnivores (46 ng mL⁻¹ vs. 17 ng mL⁻¹). Likewise, ferulic acid and other hydroxycinnamic acids were more abundant in PBD groups, likely reflecting higher intake of whole grains, vegetables, and other fiber-rich plant foods. Although urinary levels were lower than dietary intakes, this is consistent with the extensive metabolism of these compounds.⁴⁷ The EPIC-Oxford study also reported higher fiber intake in vegans compared with omnivores, supporting the notion of greater exposure to phenolic derivatives.³³ Higher vanillic and homovanillic acid levels in PBDs further support greater exposure to and metabolism of (poly)phenol-rich foods.⁴⁷

The main study limitations of this study were: (i) the use of an FFQ. This tool assesses intakes based on a predefined list of food items and may, in some cases, group foods with similar, though not identical, characteristics. This allows (poly)phenol estimation, albeit with some degree of error. Furthermore, the Phenol-Explorer (poly)phenol assignment to each item entailed some constraints. For example, some items were not available and for others, deconvolution factors to disaggregate grouped items had to be applied. (ii) Retention factors related to culinary processing were not considered,²⁵ as this information was not available. (iii) Dietary (poly)phenol intake was estimated exclusively using the Phenol-Explorer database. The USDA database was discarded to avoid inconsistencies arising from differences in food composition data (*e.g.* daidzein per 100 g of tofu in Phenol-Explorer is 1.4 mg, while in USDA, the amount increases to 10.3 mg). (iv) Urinary (poly)phenol markers were measured in first-morning urine samples rather than in 24 hour collections. Therefore, urinary concentrations reflect recent and cumulative (poly)phenol intake over the preceding hours; however, this approach is an accepted measure of (poly)phenol exposure with reduced intra-individual variability.^{48,49} (v) The sample size ($n = 200$) was calculated to achieve 80% statistical power to detect correlations > 0.2 ; however, this sample size might be limited in subgroup analyses.

Regarding strengths, the use of a validated FFQ,²⁰ expanded to include more than 30 additional plant-based food items—such as berries and soy-derived products—enabled a detailed quantification of (poly)phenol intake. This study therefore provides a comprehensive estimation of dietary (poly)phenol intake across PBDs, also including pro-vegetarians, which represents a novel aspect of our study. In addition, urinary (poly)phenol concentrations were measured, allowing us to demonstrate correlations between dietary and urinary excretion. Moreover, to the best of our knowledge, urinary (poly)phenol-based clusters—mainly driven by genistein and daidzein in plant-based diets—have not been previously described.



5. Conclusion

PBDs including vegan, pesco-, ovo-lacto- and pro-vegetarian dietary patterns showed higher dietary intake, urinary concentrations and adherence to (poly)phenol intake scores compared with omnivorous diets. Food contributions to total (poly)phenols varied among the diet groups with vegetables, legumes, fruits, nuts, PB beverages, chocolate, and spices being the most relevant (poly)phenol food sources in PBDs. Distinct (poly)phenol intake profiles across PBDs and non-PBDs reflect differences in these contributing foods. Furthermore, genistein and daidzein emerge as stable biomarkers of legume and soy-derived intake and can be regarded as indicators of PB dietary patterns. Further studies in both animal models and humans are needed to validate our findings.

Author contributions

ECA: investigation, writing – original draft, methodology, validation, writing – review and editing, data curation, formal analysis, and software. NRM: formal analysis, investigation, and writing – review and editing. PKR and JM: formal analysis, investigation, and writing – review and editing. AAS and MRB: data acquisition, data curation, investigation, and writing – review and editing. All authors: investigation and writing – review and editing. RZR and ACP: investigation, supervision, writing – review and editing, and methodology. EMM: investigation, methodology, writing – review and editing, project administration, funding acquisition, data curation, formal analysis, and supervision.

Conflicts of interest

There are no conflicts to declare.

Disclaimer

Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer/World Health Organization.

Abbreviations

BMI	Body mass index
EPIC	European Prospective Investigation into Cancer and Nutrition
FL	Factor loading
FFQ	Food frequency questionnaires
hPDI	Healthy plant-based diet index

IQR	Interquartile range
KW	Kruskal–Wallis
LOD	Limit of detection
LLOQ	Limit of quantification
PBS	Phosphate buffer solution
PB	Plant-based
PBD	Plant-based diet
PPS	(Poly)phenol-rich diet score
PCA	Principal component analysis
PC-PR ²	Principal component partial <i>R</i> -squared
stdβ	Standardized beta coefficients
rho	Spearman's correlation coefficient
SD	Standard deviation

Data availability

The data supporting this study are not publicly available due to ethical and privacy restrictions, as participants provided informed consent allowing data sharing only within the research group. Data may be made available from the corresponding author upon reasonable request and subject to approval by the relevant ethics committee.

Supplementary information (SI) is available. See DOI: <https://doi.org/10.1039/d6fo01259k>.

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