

Table S1. Baseline characteristics and relative urinary hesperidin values of participants in the first phase of the study.

Variable	Mean \pm SD
Age, <i>years</i>	41.9 \pm 12.4
Females, %	43.8%
Systolic blood pressure, <i>mm Hg</i>	121 \pm 12.4
Diastolic blood pressure, <i>mm Hg</i>	75 \pm 10.2
Weight, <i>kg</i>	75.5 \pm 14.7
Body mass index, <i>kg/m²</i>	26.1 \pm 4.08
Waist circumference, <i>cm</i>	89.3 \pm 13.7
Glucose, <i>mg/dL</i>	92.6 \pm 11.2
Cholesterol, <i>mg/dL</i>	
Total	184 \pm 43.9
LDL	110 \pm 35.9
HDL	59.7 \pm 15.6
Triglycerides, <i>mg/dL</i>	82.1 \pm 40.7
Hemoglobin, <i>g/dL</i>	14.5 \pm 0.951
Creatinine, <i>mg/dL</i>	0.919 \pm 0.191
Total bilirubin, <i>mg/dL</i>	0.719 \pm 0.740
Aspartate aminotransferase, <i>UI/L</i>	20 \pm 4.24
Alanine aminotransferase, <i>UI/L</i>	21 \pm 10
Gamma glutamyl transferase, <i>UI/L</i>	18.1 \pm 11.0
Alkaline phosphatase, <i>UI/L</i>	64.3 \pm 18.7
Thyrotropin, <i>mUI/mL</i>	1.89 \pm 0.938
Hesperidin excretion (%) (N=28)	2.67 \pm 1.79
High excretors (N=4)	6.06 \pm 1.46
Intermediate excretors (%; N=21)	2.31 \pm 1.01
Low excretors (%; N=3)	0.743 \pm 0.112

LDL, low density lipoproteins; HDL, high density lipoproteins. N=30.

Table S2. Quantities of Hesperidin metabolites and Hesperidin catabolites in urine before and after Hesperidin epimeric mixture (HEM) ingestion.

Variable	0 h	0-3 h	3-6 h	6-8 h	8-24 h
Metabolites, μmol					
Hesperetin 7,3'-di-O-glucuronide	0.001 \pm 0.001	0.001 \pm 0.001	0.046 \pm 0.021	0.41 \pm 0.11	2.79 \pm 0.51
Naringenin 7-O-glucuronide	0.017 \pm 0.005	0.018 \pm 0.005	0.007 \pm 0.003	0.039 \pm 0.010	0.17 \pm 0.08
Naringenin 4-O-glucuronide	0.033 \pm 0.012	0.035 \pm 0.011	0.006 \pm 0.003	0.083 \pm 0.028	0.34 \pm 0.18
Hesperetin 7-O-glucuronide	0.005 \pm 0.002	0.007 \pm 0.003	0.073 \pm 0.033	0.68 \pm 0.18	3.00 \pm 0.53
Hesperetin 3-O-glucuronide	0.025 \pm 0.007	0.064 \pm 0.005	0.46 \pm 0.16	5.10 \pm 1.99	23.3 \pm 3.7
Hesperetin 7-O-sulfate	0.002 \pm 0.001	0.007 \pm 0.000	0.033 \pm 0.009	0.35 \pm 0.10	1.52 \pm 0.30
Hesperetin	0.0001 \pm 0.0000	0.001 \pm 0.000	0.001 \pm 0.000	0.006 \pm 0.002	0.092 \pm 0.014
Catabolites, μmol					
2-Hydroxy-2-(4'-hydroxyphenyl)acetic acid	1.38 \pm 0.16	2.99 \pm 0.34	2.77 \pm 0.39	3.09 \pm 0.35	13.7 \pm 1.9
2-Hydroxy-2-(4'-hydroxy-3'-methoxyphenyl)acetic acid	1.09 \pm 0.08	2.89 \pm 0.23	1.76 \pm 0.15	1.98 \pm 0.27	9.38 \pm 0.90
4'-Hydroxyhippuric acid	1.81 \pm 0.24	3.65 \pm 0.59	1.84 \pm 0.19	3.51 \pm 0.59	20.3 \pm 2.5
3'-Hydroxyhippuric acid	5.14 \pm 1.77	8.34 \pm 3.40	1.89 \pm 0.55	3.56 \pm 2.28	31.9 \pm 7.2
33-Hydroxy-3-(3'-hydroxyphenyl)propanoic acid	19.6 \pm 8.0	29.0 \pm 13.9	7.36 \pm 2.64	18.0 \pm 12.8	114 \pm 26
3-(3'-hydroxyphenyl)propanoic acid-4'-sulfate	0.23 \pm 0.03	0.48 \pm 0.07	0.15 \pm 0.03	0.18 \pm 0.05	1.52 \pm 0.22
3-(3'-hydroxyphenyl)propanoic acid-4'-glucuronide	0.028 \pm 0.003	0.066 \pm 0.005	0.058 \pm 0.005	0.053 \pm 0.004	0.54 \pm 0.23
3-(4'-hydroxyphenyl)propanoic acid-3'-sulfate	0.57 \pm 0.23	0.35 \pm 0.14	0.15 \pm 0.06	0.22 \pm 0.17	3.72 \pm 1.58
Hippuric acid	24.4 \pm 3.4	56.9 \pm 9.2	40.0 \pm 4.5	41.0 \pm 6.4	193 \pm 20
3-(4'-hydroxyphenyl)propanoic acid-3-glucuronide	0.14 \pm 0.02	0.30 \pm 0.04	0.15 \pm 0.02	0.16 \pm 0.03	1.28 \pm 0.26
4'-Hydroxyphenylacetic acid	44.5 \pm 5.3	117 \pm 29	57.8 \pm 10.5	63.5 \pm 12.2	460 \pm 71
3-(4-hydroxy-3'-methoxyphenyl)propanoic acid-4'-sulfate	0.50 \pm 0.13	0.44 \pm 0.09	0.10 \pm 0.04	0.59 \pm 0.42	3.91 \pm 0.76
3-Phenylpropanoic acid-3'-sulfate	0.39 \pm 0.15	0.60 \pm 0.28	0.17 \pm 0.06	0.32 \pm 0.20	2.13 \pm 0.45
3-Phenylpropanoic acid-4'-glucuronide	0.039 \pm 0.013	0.060 \pm 0.021	0.035 \pm 0.006	0.046 \pm 0.015	0.32 \pm 0.11
3-(4-hydroxy 3'-methoxyphenyl)propanoic acid-4'-glucuronide	0.11 \pm 0.03	0.11 \pm 0.02	0.07 \pm 0.01	0.12 \pm 0.05	0.85 \pm 0.12
3-Methoxy-4-hydroxybenzoic acid	0.43 \pm 0.23	0.95 \pm 0.47	0.30 \pm 0.07	0.48 \pm 0.10	5.83 \pm 2.77
3-(3-hydroxy4'-methoxyphenyl)propanoic acid-3'-sulfate	0.016 \pm 0.008	0.021 \pm 0.012	0.006 \pm 0.004	0.27 \pm 0.13	3.75 \pm 0.86
3'-Hydroxyphenylacetic acid	23.0 \pm 4.5	58.8 \pm 12.2	34.9 \pm 6.3	32.2 \pm 6.5	171 \pm 32
4'-Hydroxy-3'-methoxyphenylacetic acid	5.19 \pm 0.60	12.5 \pm 1.6	6.86 \pm 0.74	7.02 \pm 1.03	40.5 \pm 5.0
3-(3-hydroxy 4'-methoxyphenyl)propanoic-3'-glucuronide	0.002 \pm 0.001	0.004 \pm 0.002	0.003 \pm 0.001	0.053 \pm 0.022	0.62 \pm 0.18
3-(4'-hydroxyphenyl)propanoic acid	0.005 \pm 0.002	0.024 \pm 0.009	0.014 \pm 0.005	0.016 \pm 0.004	0.089 \pm 0.027
4'-Hydroxycinnamic acid	0.013 \pm 0.008	0.017 \pm 0.016	0.004 \pm 0.002	0.057 \pm 0.019	0.28 \pm 0.16
3-(3'-hydroxyphenyl)propanoic acid	0.056 \pm 0.011	0.11 \pm 0.01	0.065 \pm 0.010	0.17 \pm 0.04	0.64 \pm 0.09
3-(3'-methoxy-4'-hydroxyphenyl)propanoic acid	0.11 \pm 0.05	0.16 \pm 0.05	0.11 \pm 0.03	0.32 \pm 0.12	1.50 \pm 0.49
3-(3'-hydroxy-4'-methoxyphenyl)propanoic acid	0.022 \pm 0.003	0.049 \pm 0.006	0.028 \pm 0.003	0.049 \pm 0.011	0.36 \pm 0.06
3',4'-dimethoxyphenylacetic acid	44.1 \pm 13.6	48 \pm 8	22.8 \pm 2.0	30.3 \pm 4.5	194 \pm 21
4'-Methoxycinnamic acid-3'-glucuronide	0.054 \pm 0.018	0.15 \pm 0.08	0.06 \pm 0.01	0.16 \pm 0.06	1.78 \pm 0.33
3-Hydroxy-3-(3'-hydroxy-4'-methoxyphenyl)propanoic acid	0.43 \pm 0.14	0.48 \pm 0.20	0.69 \pm 0.26	7.93 \pm 2.97	66.6 \pm 12.8

Data expressed as mean \pm standard deviation.

Table S3. Quantities of Hesperidin metabolites and Hesperidin catabolites in urine before and after Micronised Hesperidin epimeric mixture (MHM) ingestion.

Variable	0 h	0-3 h	3-6 h	6-8 h	8-24 h
<i>Metabolites, μmol</i>					
Hesperetin 7,3'-di-O-glucuronide	0 \pm 0	0.001 \pm 0.001	0.041 \pm 0.019	0.82 \pm 0.23	4.66 \pm 0.78
Naringenin 7-O-glucuronide	0.005 \pm 0.002	0.009 \pm 0.003	0.017 \pm 0.006	0.11 \pm 0.04	0.28 \pm 0.06
Naringenin 4-O-glucuronide	0.007 \pm 0.003	0.014 \pm 0.006	0.016 \pm 0.006	0.16 \pm 0.03	0.49 \pm 0.12
Hesperetin 7-O-glucuronide	0.004 \pm 0.002	0.004 \pm 0.002	0.075 \pm 0.033	1.62 \pm 0.47	4.24 \pm 0.68
Hesperetin 3-O-glucuronide	0.019 \pm 0.002	0.095 \pm 0.013	0.49 \pm 0.16	13.6 \pm 4.2	37.7 \pm 8.0
Hesperetin 7-O-sulfate	0.001 \pm 0.000	0.010 \pm 0.001	0.044 \pm 0.015	0.95 \pm 0.31	2.45 \pm 0.53
Hesperetin	0 \pm 0	0.001 \pm 0.000	0.002 \pm 0.000	0.014 \pm 0.004	0.12 \pm 0.02
<i>Catabolites, μmol</i>					
2-Hydroxy-2-(4' -hydroxyphenyl)acetic acid	1.53 \pm 0.15	3.28 \pm 0.38	3.62 \pm 0.48	3.02 \pm 0.30	17.7 \pm 3.2
2-Hydroxy-2-(4' -hydroxy-3' -methoxyphenyl)acetic acid	1.11 \pm 0.09	2.49 \pm 0.26	2.13 \pm 0.30	2.41 \pm 0.34	9.86 \pm 0.60
4'-Hydroxyhippuric acid	2.05 \pm 0.35	3.68 \pm 0.52	3.14 \pm 0.49	4.43 \pm 0.52	18.1 \pm 1.9
3'-Hydroxyhippuric acid	5.62 \pm 2.74	9.62 \pm 5.83	7.79 \pm 5.82	6.04 \pm 2.85	36.0 \pm 10.6
33-Hydroxy-3-(3' -hydroxyphenyl)propanoic acid	24.5 \pm 14.9	39 \pm 27	33.8 \pm 26.6	24.6 \pm 14.0	131 \pm 47
3-(3'-hydroxyphenyl)propanoic acid-4'-sulfate	0.21 \pm 0.02	0.34 \pm 0.06	0.19 \pm 0.04	0.25 \pm 0.06	1.46 \pm 0.18
3-(3'-hydroxyphenyl)propanoic acid-4'-glucuronide	0.024 \pm 0.002	0.072 \pm 0.007	0.073 \pm 0.004	0.066 \pm 0.012	0.25 \pm 0.02
3-(4'-hydroxyphenyl)propanoic acid-3'-sulfate	0.27 \pm 0.09	0.26 \pm 0.08	0.14 \pm 0.02	0.14 \pm 0.04	1.21 \pm 0.31
Hippuric acid	26.9 \pm 4.2	66.4 \pm 11.8	67.0 \pm 10.4	48.6 \pm 6.2	215 \pm 16
3-(4'-hydroxyphenyl)propanoic acid-3-glucuronide	0.13 \pm 0.02	0.30 \pm 0.04	0.22 \pm 0.03	0.21 \pm 0.03	0.97 \pm 0.06
4'-Hydroxyphenylacetic acid	51.5 \pm 6.6	74.5 \pm 17.9	64.3 \pm 8.4	77.1 \pm 11.8	439 \pm 91
3-(4-hydroxy-3'-methoxyphenyl)propanoic acid-4'-sulfate	0.28 \pm 0.07	0.46 \pm 0.13	0.11 \pm 0.05	0.37 \pm 0.09	2.60 \pm 0.52
3-Phenylpropanoic acid-3'-sulfate	0.45 \pm 0.25	0.60 \pm 0.34	0.60 \pm 0.46	0.49 \pm 0.25	2.57 \pm 0.85
3-Phenylpropanoic acid-4'-glucuronide	0.065 \pm 0.032	0.10 \pm 0.04	0.087 \pm 0.041	0.059 \pm 0.022	0.40 \pm 0.16
3-(4-hydroxy 3'-methoxyphenyl)propanoic acid-4'-glucuronide	0.060 \pm 0.014	0.13 \pm 0.03	0.10 \pm 0.02	0.11 \pm 0.02	0.62 \pm 0.11
3-Methoxy-4-hydroxybenzoic acid	0.38 \pm 0.15	0.42 \pm 0.09	0.33 \pm 0.06	0.67 \pm 0.17	5.98 \pm 3.96
3-(3-hydroxy4'-methoxyphenyl)propanoic acid-3'-sulfate	0.004 \pm 0.002	0.0003 \pm 0.0001	0.001 \pm 0.000	0.47 \pm 0.18	4.31 \pm 0.87
3'-Hydroxyphenylacetic acid	22.7 \pm 3.9	39.2 \pm 7.1	40.1 \pm 7.6	35.9 \pm 7.3	159 \pm 21
4' -Hydroxy-3' -methoxyphenylacetic acid	5.09 \pm 0.48	9.66 \pm 0.96	8.38 \pm 0.96	7.98 \pm 1.11	37.5 \pm 2.6
3-(3-hydroxy 4'-methoxyphenyl)propanoic-3'-glucuronide	0.001 \pm 0.000	0.001 \pm 0.000	0.003 \pm 0.001	0.09 \pm 0.03	0.68 \pm 0.15
3-(4'-hydroxyphenyl)propanoic acid	0.005 \pm 0.001	0.016 \pm 0.006	0.018 \pm 0.009	0.008 \pm 0.003	0.053 \pm 0.025
4'-Hydroxycinnamic acid	0.010 \pm 0.004	0.003 \pm 0.002	0.004 \pm 0.001	0.055 \pm 0.024	0.084 \pm 0.036
3-(3'-hydroxyphenyl)propanoic acid	0.15 \pm 0.08	0.12 \pm 0.04	0.12 \pm 0.03	0.20 \pm 0.03	0.76 \pm 0.13
3-(3'-methoxy-4'-hydroxyphenyl)propanoic acid	0.076 \pm 0.025	0.18 \pm 0.05	0.15 \pm 0.04	0.3 \pm 0.1	0.92 \pm 0.21
3-(3'-hydroxy-4'-methoxyphenyl)propanoic acid	0.026 \pm 0.003	0.037 \pm 0.004	0.035 \pm 0.005	0.085 \pm 0.035	0.37 \pm 0.05
3',4'-dimethoxyphenylacetic acid	23.3 \pm 4.0	29.6 \pm 3.0	29.4 \pm 3.2	32.3 \pm 3.7	183 \pm 17
4' -Methoxycinnamic acid-3' -glucuronide	0.030 \pm 0.006	0.052 \pm 0.009	0.058 \pm 0.007	0.29 \pm 0.09	2.05 \pm 0.30
3-Hydroxy-3-(3' -hydroxy-4' -methoxyphenyl)propanoic acid	0.18 \pm 0.05	0.23 \pm 0.05	0.53 \pm 0.13	13.1 \pm 3.8	87.5 \pm 15.5

Data expressed as mean \pm standard deviation.

Table S4. Quantities of Hesperidin metabolites and catabolites in urine before and after Micronised 2S-Hesperidin (M2SH) ingestion.

Variable	0 h	0-3 h	3-6 h	6-8 h	8-24 h
<i>Metabolites, μmol</i>					
Hesperetin 7,3'-di-O-glucuronide	0.004 \pm 0.004	0.004 \pm 0.003	0.069 \pm 0.027	0.36 \pm 0.09	1.77 \pm 0.39
Naringenin 7-O-glucuronide	0.014 \pm 0.003	0.025 \pm 0.010	0.030 \pm 0.009	0.077 \pm 0.016	0.23 \pm 0.06
Naringenin 4-O-glucuronide	0.024 \pm 0.007	0.044 \pm 0.019	0.063 \pm 0.018	0.20 \pm 0.04	0.38 \pm 0.09
Hesperetin 7-O-glucuronide	0.006 \pm 0.004	0.006 \pm 0.003	0.14 \pm 0.06	0.65 \pm 0.15	1.55 \pm 0.42
Hesperetin 3-O-glucuronide	0.062 \pm 0.041	0.11 \pm 0.02	0.74 \pm 0.23	3.71 \pm 1.02	15.0 \pm 4.8
Hesperetin 7-O-sulfate	0.005 \pm 0.004	0.010 \pm 0.002	0.076 \pm 0.028	0.36 \pm 0.12	1.51 \pm 0.53
Hesperetin	0.0002 \pm 0.0001	0.001 \pm 0.000	0.002 \pm 0.000	0.009 \pm 0.002	0.054 \pm 0.013
<i>Catabolites, μmol</i>					
2-Hydroxy-2-(4'-hydroxyphenyl)acetic acid	1.56 \pm 0.20	3.72 \pm 0.43	3.27 \pm 0.45	3.45 \pm 0.42	15.0 \pm 1.4
2-Hydroxy-2-(4'-hydroxy-3'-methoxyphenyl)acetic acid	1.21 \pm 0.12	2.64 \pm 0.29	2.20 \pm 0.32	2.50 \pm 0.35	10.3 \pm 1.0
4'-Hydroxyhippuric acid	2.49 \pm 0.85	4.14 \pm 0.63	3.15 \pm 0.56	4.90 \pm 0.71	17.6 \pm 1.4
3'-Hydroxyhippuric acid	5.61 \pm 3.25	10.2 \pm 4.8	8.32 \pm 5.42	10.6 \pm 6.2	43.7 \pm 8.9
33-Hydroxy-3-(3'-hydroxyphenyl)propanoic acid	24.3 \pm 16.4	34.8 \pm 18.6	29.6 \pm 19.6	40.0 \pm 25.3	157 \pm 40
3-(3'-hydroxyphenyl)propanoic acid-4'-sulfate	0.27 \pm 0.04	0.43 \pm 0.09	0.23 \pm 0.05	0.29 \pm 0.07	2.82 \pm 1.37
3-(3'-hydroxyphenyl)propanoic acid-4'-glucuronide	0.036 \pm 0.008	0.082 \pm 0.009	0.072 \pm 0.009	0.077 \pm 0.012	1.95 \pm 1.26
3-(4'-hydroxyphenyl)propanoic acid-3'-sulfate	0.35 \pm 0.14	0.55 \pm 0.26	0.22 \pm 0.06	0.32 \pm 0.15	3.50 \pm 2.13
Hippuric acid	24.5 \pm 4.0	65.2 \pm 8.2	52 \pm 6	61.7 \pm 9.2	218 \pm 11
3-(4'-hydroxyphenyl)propanoic acid-3-glucuronide	0.14 \pm 0.01	0.31 \pm 0.05	0.19 \pm 0.02	0.26 \pm 0.05	2.57 \pm 1.05
4'-Hydroxyphenylacetic acid	44.1 \pm 8.3	77.0 \pm 17.4	53.0 \pm 9.3	76.1 \pm 17.6	385 \pm 61
3-(4-hydroxy-3'-methoxyphenyl)propanoic acid-4'-sulfate	0.33 \pm 0.08	0.63 \pm 0.22	0.28 \pm 0.10	0.36 \pm 0.09	4.67 \pm 1.53
3-Phenylpropanoic acid-3'-sulfate	0.56 \pm 0.35	0.79 \pm 0.32	0.56 \pm 0.34	1.07 \pm 0.70	3.33 \pm 0.74
3-Phenylpropanoic acid-4'-glucuronide	0.054 \pm 0.038	0.070 \pm 0.024	0.080 \pm 0.036	0.12 \pm 0.07	0.48 \pm 0.20
3-(4-hydroxy 3'-methoxyphenyl)propanoic acid-4'-glucuronide	0.066 \pm 0.011	0.14 \pm 0.03	0.11 \pm 0.02	0.11 \pm 0.02	1.19 \pm 0.47
3-Methoxy-4-hydroxybenzoic acid	0.23 \pm 0.12	0.58 \pm 0.17	0.36 \pm 0.08	0.68 \pm 0.22	13.5 \pm 6.1
3-(3-hydroxy4'-methoxyphenyl)propanoic acid-3'-sulfate	0.14 \pm 0.14	0.05 \pm 0.04	0.13 \pm 0.05	1.17 \pm 0.44	10.7 \pm 2.1
3'-Hydroxyphenylacetic acid	24.1 \pm 3.4	46.9 \pm 7.4	39.8 \pm 5.3	36.4 \pm 5.3	182 \pm 29
4'-Hydroxy-3'-methoxyphenylacetic acid	6.22 \pm 0.68	12.1 \pm 1.3	9.16 \pm 0.93	9.10 \pm 0.94	56.1 \pm 16.6
3-(3-hydroxy 4'-methoxyphenyl)propanoic acid-3'-glucuronide	0.012 \pm 0.010	0.006 \pm 0.003	0.024 \pm 0.009	0.18 \pm 0.06	1.51 \pm 0.32
3-(4'-hydroxyphenyl)propanoic acid	0.022 \pm 0.016	0.025 \pm 0.011	0.029 \pm 0.011	0.016 \pm 0.005	0.069 \pm 0.025
4'-Hydroxycinnamic acid	0.018 \pm 0.011	0.012 \pm 0.006	0.006 \pm 0.003	0.043 \pm 0.011	0.10 \pm 0.03
3-(3'-hydroxyphenyl)propanoic acid	0.065 \pm 0.016	0.12 \pm 0.02	0.095 \pm 0.016	0.20 \pm 0.02	0.76 \pm 0.15
3-(3'-methoxy-4'-hydroxyphenyl)propanoic acid	0.078 \pm 0.046	0.21 \pm 0.06	0.31 \pm 0.15	0.27 \pm 0.07	1.09 \pm 0.22
3-(3'-hydroxy-4'-methoxyphenyl)propanoic acid	0.025 \pm 0.004	0.041 \pm 0.006	0.031 \pm 0.006	0.091 \pm 0.034	0.55 \pm 0.08
3',4'-dimethoxyphenylacetic acid	23.5 \pm 4.6	32.9 \pm 3.1	25.0 \pm 3.2	32.9 \pm 2.9	182 \pm 18
4'-Methoxycinnamic acid-3'-glucuronide	0.093 \pm 0.063	0.12 \pm 0.04	0.13 \pm 0.03	0.50 \pm 0.17	4.01 \pm 0.73
3-Hydroxy-3-(3'-hydroxy-4'-methoxyphenyl)propanoic acid	1.57 \pm 1.31	1.16 \pm 0.59	3.63 \pm 1.73	23.8 \pm 7.7	155 \pm 23

Data expressed as mean \pm standard deviation.

Table S5. Concentration of Hesperidin metabolites and catabolites in serum before and after Hesperidin epimeric mixture (HEM) ingestion.

Variable	0 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	24 h
<i>Metabolites, μM</i>									
Hesperetin, 7,3,di-O-Glucuronide	0.001 \pm 0.000	0.001 \pm 0.000	0.001 \pm 0.000	0.002 \pm 0.004	0.004 \pm 0.009	0.014 \pm 0.017	0.029 \pm 0.025	0.040 \pm 0.029	0.013 \pm 0.021
Hesperetin 7-O-Glucuronide	0.0003 \pm 0.0000	0.0003 \pm 0.0000	0.0003 \pm 0.0000	0.003 \pm 0.007	0.018 \pm 0.024	0.054 \pm 0.059	0.083 \pm 0.070	0.084 \pm 0.052	0.028 \pm 0.055
Hesperetin 3-O-Glucuronide	0.001 \pm 0.000	0.001 \pm 0.000	0.003 \pm 0.008	0.012 \pm 0.017	0.030 \pm 0.039	0.085 \pm 0.096	0.13 \pm 0.12	0.15 \pm 0.12	0.057 \pm 0.086
Hesperetin 7-O-Sulfate	0.0001 \pm 0.0003	0.0003 \pm 0.0005	0.001 \pm 0.002	0.004 \pm 0.007	0.012 \pm 0.016	0.085 \pm 0.084	0.086 \pm 0.065	0.086 \pm 0.049	0.026 \pm 0.042
Hesperetin	0.0003 \pm 0.0008	0.0001 \pm 0.0000	0.0001 \pm 0.0000	0.0001 \pm 0.0000	0.0001 \pm 0.0000	0.001 \pm 0.001	0.0004 \pm 0.0010	0.001 \pm 0.001	0.0001 \pm 0.0001
<i>Catabolites, μM</i>									
2-Hydroxy-2-(4' -hydroxy-3' -methoxyphenyl)acetic acid	0.028 \pm 0.007	0.024 \pm 0.008	0.024 \pm 0.007	0.024 \pm 0.008	0.025 \pm 0.007	0.028 \pm 0.008	0.025 \pm 0.005	0.024 \pm 0.008	0.029 \pm 0.008
4'-Hydroxyhippuric acid	0.022 \pm 0.008	0.016 \pm 0.008	0.014 \pm 0.007	0.014 \pm 0.007	0.014 \pm 0.007	0.028 \pm 0.009	0.026 \pm 0.007	0.022 \pm 0.006	0.034 \pm 0.023
3'-Hydroxyhippuric acid	0.065 \pm 0.090	0.040 \pm 0.058	0.030 \pm 0.037	0.024 \pm 0.028	0.017 \pm 0.017	0.019 \pm 0.014	0.028 \pm 0.017	0.032 \pm 0.021	0.11 \pm 0.07
3-Hydroxy-3-(3' -hydroxyphenyl)propanoic acid	0.11 \pm 0.24	0.035 \pm 0.088	0.029 \pm 0.065	0.021 \pm 0.058	0.017 \pm 0.042	0.026 \pm 0.053	0.028 \pm 0.048	0.045 \pm 0.063	0.27 \pm 0.24
Hippuric acid	1.18 \pm 0.82	0.69 \pm 0.49	0.59 \pm 0.42	0.57 \pm 0.39	0.56 \pm 0.37	0.63 \pm 0.29	0.58 \pm 0.28	0.53 \pm 0.25	1.44 \pm 0.69
4'-Hydroxyphenylacetic acid	4.40 \pm 5.29	3.83 \pm 3.59	3.35 \pm 2.75	3.04 \pm 2.59	2.64 \pm 1.52	3.54 \pm 2.08	3.51 \pm 2.11	3.30 \pm 1.97	4.78 \pm 4.03
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid - 4'-sulfate	0.006 \pm 0.005	0.003 \pm 0.002	0.002 \pm 0.002	0.002 \pm 0.001	0.002 \pm 0.002	0.004 \pm 0.004	0.005 \pm 0.004	0.005 \pm 0.003	0.019 \pm 0.035
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid - 4'-glucuronide	0.003 \pm 0.002	0.002 \pm 0.001	0.002 \pm 0.001	0.001 \pm 0.001	0.001 \pm 0.001	0.002 \pm 0.002	0.003 \pm 0.002	0.003 \pm 0.002	0.008 \pm 0.009
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid - 3'-sulfate	0.001 \pm 0.001	0.0004 \pm 0.0012	0.0004 \pm 0.0012	0.001 \pm 0.001	0.002 \pm 0.003	0.006 \pm 0.008	0.016 \pm 0.018	0.022 \pm 0.020	0.024 \pm 0.026
3'-hydroxyphenylacetic acid	3.67 \pm 1.91	3.37 \pm 1.74	3.19 \pm 1.75	2.92 \pm 1.57	2.57 \pm 1.43	3.04 \pm 1.50	2.95 \pm 1.38	2.91 \pm 1.07	3.1 \pm 1.3
4' -Hydroxy-3' -methoxyphenylacetic acid	0.23 \pm 0.09	0.17 \pm 0.09	0.15 \pm 0.08	0.15 \pm 0.07	0.15 \pm 0.08	0.16 \pm 0.05	0.15 \pm 0.08	0.13 \pm 0.07	0.22 \pm 0.07
3-(3'-hydroxy-4'-methoxyphenyl)propanoic acid - 3'-glucuronide	0.0002 \pm 0.0002	0.0001 \pm 0.0002	0.0001 \pm 0.0001	0.0001 \pm 0.0001	0.0002 \pm 0.0002	0.001 \pm 0.001	0.001 \pm 0.002	0.002 \pm 0.002	0.002 \pm 0.002
3-(3'-hydroxyphenyl)propanoic acid	0.42 \pm 0.10	0.42 \pm 0.09	0.40 \pm 0.08	0.37 \pm 0.08	0.36 \pm 0.09	0.45 \pm 0.08	0.48 \pm 0.09	0.46 \pm 0.09	0.41 \pm 0.14
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid	0.026 \pm 0.019	0.015 \pm 0.010	0.010 \pm 0.006	0.009 \pm 0.007	0.011 \pm 0.010	0.028 \pm 0.027	0.034 \pm 0.028	0.03 \pm 0.02	0.086 \pm 0.141
3-(3'-hydroxyphenyl-4'-methoxyphenyl)propionic acid	0.010 \pm 0.021	0.007 \pm 0.015	0.007 \pm 0.016	0.016 \pm 0.024	0.041 \pm 0.059	0.18 \pm 0.23	0.31 \pm 0.33	0.35 \pm 0.31	0.2 \pm 0.2
3 Phenylpropanoic acid	0.49 \pm 0.29	0.50 \pm 0.37	0.45 \pm 0.31	0.38 \pm 0.27	0.34 \pm 0.24	0.50 \pm 0.38	0.50 \pm 0.39	0.47 \pm 0.35	0.73 \pm 0.47
4' -Methoxycinnamic acid-3' -glucuronide	0.001 \pm 0.001	0.001 \pm 0.001	0.001 \pm 0.001	0.0004 \pm 0.0005	0.0004 \pm 0.0005	0.001 \pm 0.001	0.002 \pm 0.002	0.003 \pm 0.003	0.007 \pm 0.008

Data expressed as mean \pm standard deviation.

Table S6. Concentration of Hesperidin metabolites and catabolites in serum before and after Micronised Hesperidin epimeric mixture (MHEM) ingestion.

Variable	0 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	24 h
<i>Metabolites, μM</i>									
Hesperetin, 7,3,di-O-Glucuronide	0.001 \pm 0.000	0.001 \pm 0.000	0.001 \pm 0.000	0.001 \pm 0.002	0.001 \pm 0.004	0.018 \pm 0.021	0.061 \pm 0.060	0.061 \pm 0.056	0.026 \pm 0.038
Hesperetin 7-O-Glucuronide	0.0005 \pm 0.0009	0.001 \pm 0.002	0.001 \pm 0.003	0.003 \pm 0.005	0.021 \pm 0.027	0.092 \pm 0.091	0.17 \pm 0.16	0.14 \pm 0.13	0.046 \pm 0.075
Hesperetin 3-O-Glucuronide	0.001 \pm 0.000	0.001 \pm 0.000	0.001 \pm 0.000	0.008 \pm 0.016	0.037 \pm 0.041	0.11 \pm 0.08	0.27 \pm 0.27	0.22 \pm 0.20	0.071 \pm 0.094
Hesperetin 7-O-Sulfate	0.0001 \pm 0.0002	0.001 \pm 0.000	0.001 \pm 0.001	0.005 \pm 0.008	0.022 \pm 0.036	0.16 \pm 0.20	0.28 \pm 0.31	0.21 \pm 0.20	0.054 \pm 0.078
Hesperetin	0.0001 \pm 0.0000	0.0001 \pm 0.0000	0.0001 \pm 0.0000	0.0001 \pm 0.0000	0.0002 \pm 0.0006	0.002 \pm 0.003	0.003 \pm 0.005	0.002 \pm 0.003	0.001 \pm 0.001
<i>Catabolites, μM</i>									
2-Hydroxy-2-(4' -hydroxy-3' -methoxyphenyl)acetic acid	0.029 \pm 0.007	0.027 \pm 0.007	0.024 \pm 0.007	0.023 \pm 0.009	0.025 \pm 0.007	0.028 \pm 0.008	0.023 \pm 0.010	0.024 \pm 0.005	0.029 \pm 0.006
4'-Hydroxyhippuric acid	0.026 \pm 0.010	0.019 \pm 0.008	0.016 \pm 0.006	0.014 \pm 0.005	0.015 \pm 0.005	0.034 \pm 0.014	0.032 \pm 0.015	0.025 \pm 0.005	0.033 \pm 0.011
3'-Hydroxyhippuric acid	0.048 \pm 0.046	0.034 \pm 0.031	0.031 \pm 0.025	0.024 \pm 0.018	0.021 \pm 0.017	0.029 \pm 0.020	0.044 \pm 0.032	0.062 \pm 0.054	0.14 \pm 0.24
3-Hydroxy-3-(3' -hydroxyphenyl)propanoic acid	0.073 \pm 0.141	0.028 \pm 0.060	0.033 \pm 0.058	0.039 \pm 0.052	0.032 \pm 0.055	0.025 \pm 0.051	0.070 \pm 0.119	0.11 \pm 0.18	0.38 \pm 0.77
Hippuric acid	1.15 \pm 0.49	0.76 \pm 0.37	0.66 \pm 0.28	0.61 \pm 0.22	0.58 \pm 0.19	0.71 \pm 0.21	0.64 \pm 0.24	0.67 \pm 0.27	1.58 \pm 1.60
4'-Hydroxyphenylacetic acid	4.06 \pm 3.71	3.69 \pm 3.04	3.31 \pm 2.43	3.06 \pm 2.09	2.71 \pm 1.85	3.99 \pm 2.36	4.08 \pm 3.30	4.18 \pm 3.94	4.17 \pm 3.34
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid - 4'-sulfate	0.007 \pm 0.006	0.005 \pm 0.005	0.003 \pm 0.003	0.002 \pm 0.003	0.002 \pm 0.003	0.005 \pm 0.005	0.006 \pm 0.006	0.006 \pm 0.003	0.010 \pm 0.008
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid - 4'-glucuronide	0.003 \pm 0.004	0.003 \pm 0.004	0.002 \pm 0.003	0.002 \pm 0.002	0.002 \pm 0.002	0.003 \pm 0.003	0.004 \pm 0.004	0.004 \pm 0.003	0.006 \pm 0.006
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid - 3'-sulfate	0.0001 \pm 0.0003	0.0002 \pm 0.0005	0.0002 \pm 0.0004	0.0002 \pm 0.0005	0.001 \pm 0.002	0.007 \pm 0.008	0.029 \pm 0.029	0.041 \pm 0.041	0.022 \pm 0.036
3'-hydroxyphenylacetic acid	3.44 \pm 1.53	3.38 \pm 1.36	3.24 \pm 1.63	2.94 \pm 1.39	2.54 \pm 1.01	3.20 \pm 1.37	3.47 \pm 1.34	3.22 \pm 1.15	3.37 \pm 1.75
4' -Hydroxy-3' -methoxyphenylacetic acid	0.24 \pm 0.10	0.19 \pm 0.10	0.17 \pm 0.08	0.16 \pm 0.06	0.15 \pm 0.07	0.19 \pm 0.09	0.19 \pm 0.10	0.17 \pm 0.14	0.23 \pm 0.11
3-(3'-hydroxy-4'-methoxyphenyl)propanoic acid - 3'-glucuronide	0.0001 \pm 0.0001	0.0001 \pm 0.0001	0.0001 \pm 0.0001	0.0001 \pm 0.0001	0.0001 \pm 0.0002	0.001 \pm 0.001	0.002 \pm 0.003	0.004 \pm 0.005	0.002 \pm 0.002
3-(3'-hydroxyphenyl)propanoic acid	0.44 \pm 0.17	0.46 \pm 0.21	0.43 \pm 0.19	0.40 \pm 0.21	0.35 \pm 0.15	0.50 \pm 0.17	0.52 \pm 0.15	0.49 \pm 0.22	0.49 \pm 0.17
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid	0.033 \pm 0.036	0.026 \pm 0.030	0.018 \pm 0.020	0.014 \pm 0.015	0.015 \pm 0.018	0.034 \pm 0.032	0.044 \pm 0.036	0.035 \pm 0.020	0.063 \pm 0.069
3-(3'-hydroxyphenyl-4'-methoxyphenyl)propionic acid	0.004 \pm 0.005	0.004 \pm 0.006	0.004 \pm 0.006	0.010 \pm 0.016	0.038 \pm 0.060	0.22 \pm 0.24	0.70 \pm 0.65	0.74 \pm 0.74	0.29 \pm 0.52
3 Phenylpropanoic acid	0.50 \pm 0.19	0.50 \pm 0.24	0.43 \pm 0.19	0.35 \pm 0.14	0.30 \pm 0.12	0.49 \pm 0.21	0.53 \pm 0.28	0.53 \pm 0.28	0.72 \pm 0.46
4' -Methoxycinnamic acid-3' -glucuronide	0.0006 \pm 0.0007	0.0005 \pm 0.0005	0.0003 \pm 0.0003	0.0002 \pm 0.0002	0.0003 \pm 0.0003	0.001 \pm 0.001	0.004 \pm 0.004	0.005 \pm 0.005	0.006 \pm 0.006

Data expressed as mean \pm standard deviation.

Table S7. Concentration of Hesperidin metabolites and catabolites in serum before and after Micronised 2S-Hesperidin (M2SH) ingestion.

Variable	0 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h	24 h
<i>Metabolites, μM</i>									
Hesperetin, 7,3,di-O-Glucuronide	0.001 \pm 0.000	0.001 \pm 0.000	0.001 \pm 0.000	0.003 \pm 0.006	0.009 \pm 0.012	0.016 \pm 0.019	0.030 \pm 0.029	0.035 \pm 0.024	0.007 \pm 0.015
Hesperetin 7-O-Glucuronide	0.0004 \pm 0.0005	0.0005 \pm 0.0009	0.002 \pm 0.004	0.008 \pm 0.014	0.022 \pm 0.033	0.032 \pm 0.034	0.049 \pm 0.045	0.054 \pm 0.043	0.009 \pm 0.020
Hesperetin 3-O-Glucuronide	0.005 \pm 0.010	0.003 \pm 0.008	0.009 \pm 0.017	0.015 \pm 0.032	0.041 \pm 0.056	0.074 \pm 0.075	0.15 \pm 0.14	0.18 \pm 0.17	0.029 \pm 0.061
Hesperetin 7-O-Sulfate	0.001 \pm 0.003	0.001 \pm 0.001	0.003 \pm 0.006	0.011 \pm 0.019	0.027 \pm 0.043	0.055 \pm 0.071	0.1 \pm 0.1	0.12 \pm 0.12	0.023 \pm 0.050
Hesperetin	0.0001 \pm 0.0000	0.0001 \pm 0.0000	0.0001 \pm 0.0000	0.0003 \pm 0.0009	0.0003 \pm 0.0008	0.0006 \pm 0.0014	0.001 \pm 0.002	0.001 \pm 0.002	0.0002 \pm 0.0007
<i>Catabolites, μM</i>									
2-Hydroxy-2-(4' -hydroxy-3' -methoxyphenyl)acetic acid	0.027 \pm 0.009	0.022 \pm 0.007	0.024 \pm 0.005	0.025 \pm 0.007	0.023 \pm 0.009	0.029 \pm 0.006	0.028 \pm 0.011	0.025 \pm 0.007	0.032 \pm 0.009
4'-Hydroxyhippuric acid	0.024 \pm 0.009	0.017 \pm 0.008	0.017 \pm 0.008	0.017 \pm 0.009	0.015 \pm 0.007	0.032 \pm 0.010	0.034 \pm 0.013	0.028 \pm 0.012	0.037 \pm 0.025
3'-Hydroxyhippuric acid	0.057 \pm 0.066	0.046 \pm 0.044	0.043 \pm 0.043	0.037 \pm 0.035	0.035 \pm 0.037	0.045 \pm 0.056	0.062 \pm 0.080	0.069 \pm 0.065	0.13 \pm 0.17
3-Hydroxy-3-(3' -hydroxyphenyl)propanoic acid	0.11 \pm 0.15	0.046 \pm 0.083	0.066 \pm 0.167	0.069 \pm 0.171	0.083 \pm 0.179	0.13 \pm 0.22	0.12 \pm 0.19	0.15 \pm 0.18	0.36 \pm 0.57
Hippuric acid	1.23 \pm 0.78	0.76 \pm 0.49	0.73 \pm 0.48	0.74 \pm 0.42	0.75 \pm 0.38	0.85 \pm 0.35	0.85 \pm 0.51	0.82 \pm 0.61	1.39 \pm 0.79
4'-Hydroxyphenylacetic acid	2.66 \pm 1.13	2.57 \pm 0.99	2.68 \pm 1.36	2.49 \pm 1.44	2.55 \pm 1.24	3.69 \pm 1.35	3.90 \pm 1.69	3.56 \pm 1.37	3.34 \pm 1.43
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid - 4'-sulfate	0.078 \pm 0.258	0.016 \pm 0.039	0.005 \pm 0.005	0.003 \pm 0.004	0.003 \pm 0.003	0.004 \pm 0.003	0.007 \pm 0.006	0.008 \pm 0.007	0.035 \pm 0.102
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid - 4'-glucuronide	0.005 \pm 0.007	0.003 \pm 0.002	0.003 \pm 0.002	0.002 \pm 0.002	0.002 \pm 0.001	0.002 \pm 0.002	0.004 \pm 0.002	0.004 \pm 0.003	0.017 \pm 0.050
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid - 3'-sulfate	0.002 \pm 0.005	0.002 \pm 0.006	0.002 \pm 0.005	0.004 \pm 0.009	0.014 \pm 0.025	0.028 \pm 0.045	0.058 \pm 0.066	0.10 \pm 0.07	0.028 \pm 0.046
3'-hydroxyphenylacetic acid	3.36 \pm 1.51	3.25 \pm 1.30	3.27 \pm 1.58	2.90 \pm 1.46	2.61 \pm 1.30	3.15 \pm 1.35	3.51 \pm 1.55	3.46 \pm 1.45	2.95 \pm 1.49
4' -Hydroxy-3' -methoxyphenylacetic acid	0.25 \pm 0.12	0.18 \pm 0.11	0.16 \pm 0.11	0.16 \pm 0.09	0.18 \pm 0.10	0.20 \pm 0.09	0.19 \pm 0.14	0.18 \pm 0.13	0.28 \pm 0.28
3-(3'-hydroxy-4'-methoxyphenyl)propanoic acid - 3'-glucuronide	0.0002 \pm 0.0003	0.0002 \pm 0.0004	0.0002 \pm 0.0003	0.0003 \pm 0.0005	0.001 \pm 0.001	0.002 \pm 0.003	0.004 \pm 0.004	0.007 \pm 0.005	0.003 \pm 0.003
3-(3'-hydroxyphenyl)propanoic acid	0.46 \pm 0.22	0.47 \pm 0.23	0.45 \pm 0.18	0.42 \pm 0.18	0.38 \pm 0.16	0.54 \pm 0.18	0.58 \pm 0.19	0.54 \pm 0.19	0.50 \pm 0.22
3-(4'-hydroxy-3'-methoxyphenyl)propanoic acid	0.034 \pm 0.029	0.029 \pm 0.031	0.021 \pm 0.021	0.017 \pm 0.017	0.017 \pm 0.014	0.028 \pm 0.017	0.056 \pm 0.050	0.053 \pm 0.051	0.17 \pm 0.48
3-(3'-hydroxyphenyl-4'-methoxyphenyl)propionic acid	0.009 \pm 0.013	0.009 \pm 0.019	0.027 \pm 0.073	0.10 \pm 0.28	0.26 \pm 0.50	0.57 \pm 0.94	1.09 \pm 1.21	1.41 \pm 1.14	0.39 \pm 0.73
3 Phenylpropanoic acid	0.51 \pm 0.32	0.58 \pm 0.37	0.51 \pm 0.36	0.47 \pm 0.30	0.41 \pm 0.27	0.56 \pm 0.32	0.63 \pm 0.41	0.60 \pm 0.38	0.71 \pm 0.41
4' -Methoxycinnamic acid-3' -glucuronide	0.001 \pm 0.002	0.001 \pm 0.002	0.001 \pm 0.002	0.001 \pm 0.001	0.002 \pm 0.002	0.003 \pm 0.003	0.005 \pm 0.004	0.007 \pm 0.005	0.008 \pm 0.010

Data expressed as mean \pm standard deviation

Table S8. Concentration of Hesperidin metabolites plus Hesperidin catabolites (nM) in serum before and after Hesperidin epimeric mixture (HEM), Micronised Hesperidin epimeric mixture (MHEM) and Micronised 2S-Hesperidin (M2SH) treatments.

Intervention	Time after ingestion									P for trend
	Baseline (0 h)	2 h	3 h	4 h	5 h	6 h	7 h	8 h	24 h	
HEM (n=13)	126	45[*]	41	58	119	448[*]	676[†]	766[‡]	624[‡]	<0.001^a
	(65)	(24)	(18)	(19)	(33)	(120)	(142)	(113)	(60)	^b 0.008
MHEM (n=14)	79	34	40	66	254[†]	650[‡]	1612[‡]	1545[‡]	913[†]	<0.001^a
	(37)	(16)	(15)	(16)	(42)	(162)	(354)	(339)	(283)	0.829
2SH (n=13)	123	63	111	215	465[*]	917[†]	1619[‡]	2084[‡]	854[†]	<0.001^a
	(43)	(29)	(72)	(139)	(217)	(336)	(398)	(327)	(298)	0.840

Data expressed as mean (standard error). Metabolites involved: Hesperetin (Hesp), 7, 3' di-O- glucuronide (gluc)+ Hesp 7-O-gluc + Hesp 3-O-gluc + Hesp 7-O-sulfate+ Hesp. Catabolites involved: isoferulic acid-3'-glucuronide + 3-(3'- hydroxy-4'-methoxyphenyl) propionic acid (Dihydro-isoferulic acid) + 3-(3'- hydroxy 4'-methoxyphenyl) propionic acid-3'-sulfate + 3-(3'- hydroxy 4'-methoxyphenyl) propionic acid-3'-O-glucuronide + 3'-(3'-hydroxyphenyl) hydracrylic acid. General Linear Model with Bonferroni correction. Data log transformed for normalization. ^{*} P<0.05, [†] P<0.01, [‡] P<0.001 *versus* baseline. P for trend: ^a linear, ^b quadratic. Significant results in **bold**.

Table S9. Concentration of Hesperidin metabolites (nM) in serum before and after Hesperidin epimeric mixture (HEM), Micronised Hesperidin epimeric mixture (MHEM) and Micronised 2S-Hesperidin (M2SH) treatments.

Intervention	Time after ingestion									P for trend
	Baseline (0 h)	2 h	3 h	4 h	5 h	6 h	7 h	8 h	24 h	
HEM (n=14)	1.64 (0.25)	1.58 (0.13)	4.29 (2.57)	20.9 (8.10)	63.4 (21.4)	239[‡] (63.3)	332[‡] (65.1)	361[‡] (58.1)	124[‡] (54)	^a<0.001 ^b 0.173
MHEM (n=14)	1.64 (0.24)	2.29[*] (0.50)	3.09 (0.82)	16.6 (7.8)	81.9[†] (26.6)	381[‡] (102)	785[‡] (201)	635[‡] (144)	198[†] (73.6)	^a<0.001 ^b 0.038
2SH (n=14)	6.50 (3.50)	4.42 (2.4)	1.46 (7.2)	35.9 (18.5)	99.7 (37.1)	177[‡] (50.8)	329[‡] (81.7)	393[‡] (89.8)	67.8 (38.6)	^a<0.001 ^b0.002

Data expressed as mean (standard error). Metabolites involved: Hesperetin (Hesp), 7, 3' di-O- glucuronide (gluc)+ Hesp 7-O-gluc + Hesp 3-O-gluc + Hesp 7-O-sulfate+ Hesp. General Linear Model with Bonferroni correction. Data log transformed for normalization. ^{*} P<0.05, [†] P<0.01, [‡] P<0.001versus baseline. P for trend: ^a linear, ^b quadratic.

Table S10. Concentration of Hesperidin catabolites (nM) in serum before and after Hesperidin epimeric mixture (HEM), Micronised Hesperidin epimeric mixture (MHEM) and Micronised 2S-Hesperidin (M2SH) treatments.

Intervention	Time after ingestion									P for trend
	Baseline (0 h)	2 h	3 h	4 h	5 h	6 h	7 h	8 h	24 h	
HEM (n=13)	124	43	37	38	60	215	357	421	495*	<0.001^a
	(65)	(25)	(18)	(16)	(19)	(67)	(97)	(89)	(80)	^b 0.119
MHEM (n=14)	77	32	37	49	71	253	801*	903*	698*	<0.001^a
	(37)	(16)	(15)	(13)	(22)	(75)	(190)	(210)	(235)	0.124
2SH (n=13)	119	59	96	177	358	718	1281*	1672*	782	<0.001^a
	(43)	(27)	(67)	(126)	(193)	(317)	(390)	(348)	(282)	0.413

Data expressed as mean (standard error). Catabolites involved: isoferulic acid-3'-glucuronide + 3-(3'- hydroxy- 4'-methoxyphenyl) propionic acid (Dihydro-isoferulic acid) + 3-(3'- hydroxy 4'-methoxyphenyl) propionic acid-3'-sulfate + 3-(3'- hydroxy 4'-methoxyphenyl) propionic acid-3'-O-glucuronide + 3'-(3'-hydroxyphenyl) hydracrylic acid . General Linear Model with Bonferroni correction. Data log transformed for normalization.* P<0.05 *versus* baseline. P for trend: a linear, ^b quadratic. Significant results in **bold**.