

Figure S1 Proposed polyphenol metabolism pathways. Red fonts reflect the parent polyphenols of mixed spices used in this study, while the red rectangle shows the aromatic acids quantified in this study.

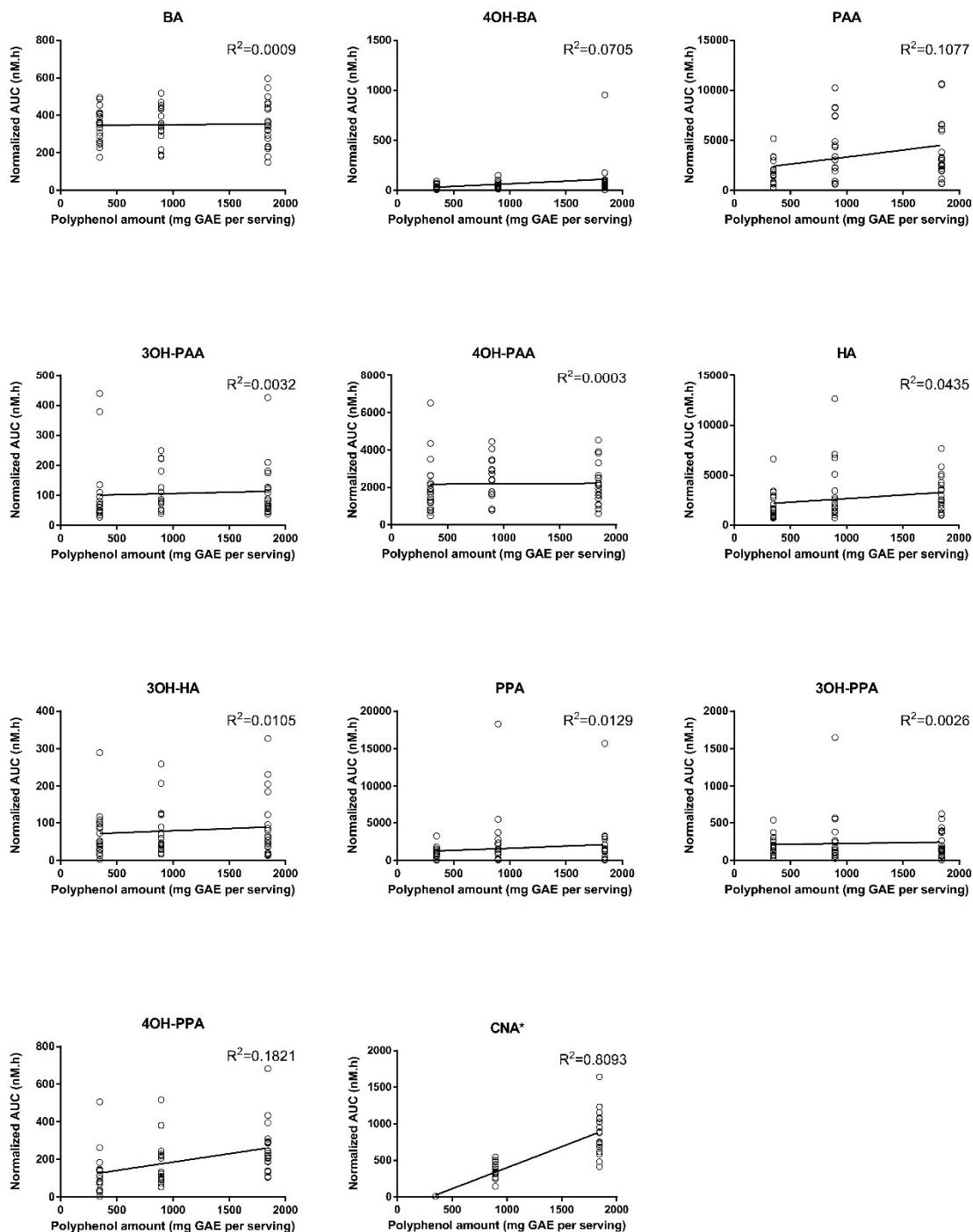


Figure S2. Scatter plot and linear regression of aromatic and phenolic acid metabolites normalized area under the curve (AUC) (nM.h) against total polyphenol content of D0C, D1C and D2C meals (mg of gallic acid equivalent (GAE) per serving) as used in the mixed spices intervention study. Benzoic acid (BA); 4-hydroxybenzoic acid (4OH-BA); phenylacetic acid (PAA); 3-hydroxyphenylacetic acid (3OH-PAA); 4-hydroxyphenylacetic acid (4OH-PAA); 3-phenylpropanoic acid (PPA); 3-(3-hydroxyphenyl)-propanoic acid (3OH-PPA); 3-(4-hydroxyphenyl)-propanoic acid (4OH-PPA), hippuric acid (HA); 3-hydroxyhippuric acid (3OH-HA); and cinnamic acid (CNA); *One outlier was omitted from the regression.

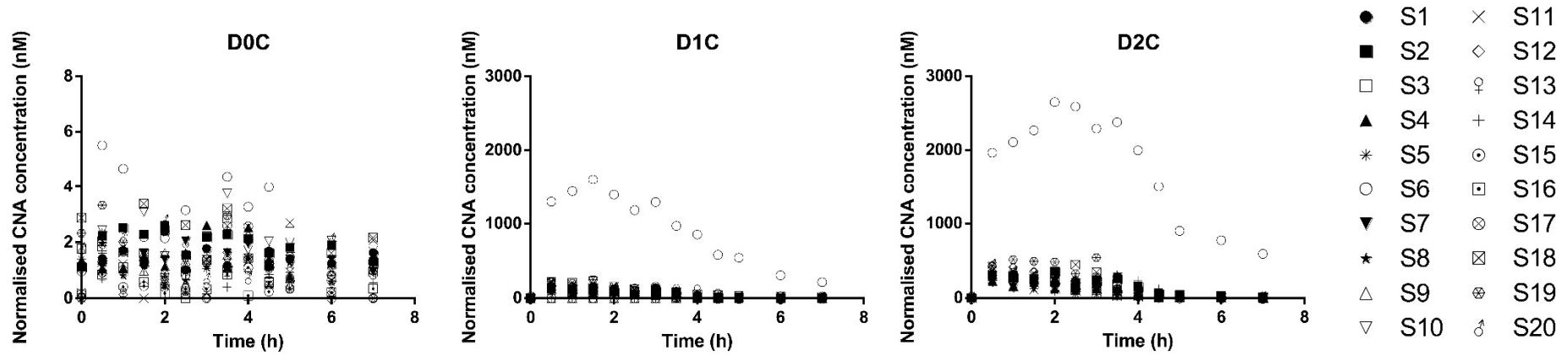


Figure S3. Normalized linear plasma concentration against time plots of cinnamic acid (CNA) across all three doses. One participant was identified as a biological outlier, displaying strong dose-exposure relationship within himself, but higher exposure relative to other participants in the study.

Table S1. List of documented polyphenols and their abundances found in the spices and vegetables used in the study. Mean polyphenol content and total polyphenol content (TPC, based on Folin assay) retrieved from Phenol-Explorer 3.6 (<http://phenol-explorer.eu/>) and expressed in mg/100mg fresh weight (FW).

Food	Food form	Polyphenol class	Polyphenol sub-class	Polyphenol	Mean content (mg/100g FW)	TPC (mg/100g FW)
Turmeric	Turmeric dried	Other polyphenols	Curcuminoids	Bisdemethoxycurcumin	1237.5	
				Curcumin	2213.57	
				Demethoxycurcumin	1982.5	
					2117	
Cumin	Cumin	Flavonoids	Flavonols	Kaempferol	38.6	
				Eriodictyol	0.3	
			Flavones	Luteolin	3.1	
		Phenolic acids	Hydroxycinnamic acid	Caffeic acid	16.6	
				Ferulic acid	5.8	
			Hydroxybenzoic acids	Gallic acid	1.2	
					2038.33	
Coriander	Coriander, seed					357.36
Cinnamon	Ceylan cinnamon	Phenolic acids	Hydroxybenzoic acids	2-Hydroxybenzoic acid	0.7	
				Protocatechuic acid	1.16	
			Hydroxycinnamic acids	Syringic acid	0.78	
				Caffeic acid	24.2	
		p-Coumaric acid	Hydroxybenzoic acids	p-Coumaric acid	0.55	
					9700	
			Phenolic acids	Eugenol	12592.93	
				Gallic acid	458.19	
Clove	Cloves	Flavonoids	Flavonols	Protocatechuic acid	0.52	
				Syringic acid	0.79	
			Phenolic acids	p-Coumaric acid	8.49	
					16047.5	
Cayenne pepper	Cayenne pepper, raw	Flavonoids	Flavones	Luteolin	1.89	
				Quercetin	2.92	
			Flavonols	Cyanidin 3-O-(6"-caffeooyl-glucoside)	0.07	
				Cyanidin 3-O-(6"-p-coumaroyl-glucoside)	0.23	
Gooseberry (amla)	Gooseberry	Flavonoids	Anthocyanins	Cyanidin 3-O-galactoside	1.18	
				Cyanidin 3-O-glucoside	0.005	
			Flavonols	Cyanidin 3-O-rutinoside	2.95	
				Peonidin 3-O-glucoside	2.03	
			Phenolic acids	Peonidin 3-O-rutinoside	0.06	
				(+)-Catechin	0.1	
				(+)-Gallocatechin	1.67	
				Kaempferol	0.44	
Garlic	Garlic fresh	Lignans	Lignans	Quercetin	0.88	
				Secoisolariciresinol	1.23	
			Flavonols	4-Hydroxybenzoic acid 4-O-glucoside	1.15	
				Protocatechuic acid 4-O-glucoside	0.45	
			Phenolic acids	3-Caffeoylquinic acid	0.35	
				3-Feruloylquinic acid	0.1	
				3-p-Coumaroylquinic acid	0.05	
				Caffeic acid 4-O-glucoside	0.2	
Ginger	Ginger, fresh	Lignans	Flavonols	Caffeoyl glucose	0.9	
				Ferulic acid 4-O-glucoside	0.3	
			Phenolic acids	p-Coumaric acid 4-O-glucoside	0.5	
				p-Coumaroyl glucose	0.7	
					470.14	
Onion	Onion (red), raw	Flavonoids	Anthocyanins	Laricresinol	17.19	
				Matairesinol	0.00248	
				Pinoresinol	12.1	
				Secoisolariciresinol	1.55	
			Flavonols		87.04	
				Isorhamnetin	1.51	
				Isorhamnetin 4'-O-glucoside	6	
				Quercetin	1.31	
Tomato	Tomato, whole, raw	Flavonoids	Flavones	Quercetin 3,4'-O-diglucoside	77.08	
				Quercetin 3-O-glucoside	1.8	
				Quercetin 3-O-rutinoside	0.21	
				Quercetin 4'-O-glucoside	38.8	
			Phenolic acids	Quercetin 7,4'-O-diglucoside	1.8	
				Kaempferol	0.99	
				Myricetin	0.46	
				Apigenin	0.3	
			Flavones	Luteolin	0.16	
				Protocatechuic acid	2	
					102.83	
				Naringenin 7-O-glucoside	0.14	
			Flavanones	Naringenin	0.96	
				Kaempferol	0.01	
				Quercetin	0.00423	

Food	Food form	Polyphenol class	Polyphenol sub-class	Polyphenol	Mean content (mg/100g FW)	TPC (mg/100g FW)
				Quercetin 3-O-rutinoside	0.14	
				Myricetin	0.04	
			Flavones	Apigenin	0.09	
		Lignans	Lignans	Laricresinol	2.1	
				Matairesinol	0.00000833	
				Medioresinol	0.0035	
				Pinoresinol	0.7	
				Secoisolariciresinol	0.05	
				Syringaresinol	0.0045	
		Phenolic acids	Hydroxycinnamic acids	4-Caffeoylquinic acid	1.17	
				5-Caffeoylquinic acid	1.84	
				Caffeic acid	0.45	
				Ferulic acid	0.27	
				p-Coumaric acid	0.13	
			Hydroxybenzoic acids	4-Hydroxybenzoic acid	0.05	
				Vanillic acid	0.02	
						45.06
Aubergine	Aubergine, peeled	Phenolic acid	Hydroxybenzoic acids	4-Hydroxybenzoic acid	0.09	
				Gallic acid	0.14	
				Protocatechuic acid	0.58	
			Hydroxycinnamic acids	Caffeic acid	0.38	
				Ferulic acid	0.22	
				p-Coumaric acid	0.08	

Table S2. Mass spectrometry compound-dependent parameters and method validation parameters, linearity (R^2), accuracy (percentage deviation from spiked), and precision (relative SD). Entrance potential was set at 10 V for all analytes. CE, collision energy; CXP, collision exit potential; DP, declustering potential; Q1, Parent mass/charge; Q3, product mass/charge; RT, retention time.

Polyphenols	Q1	Q3	RT (min)	Dwell (msec)	DP	CE	CXP	Dynamic range (nM)	Linearity R^2	Spiked amount (nM)	Accuracy (%)	Precision (%)
Benzoic acid derivatives												
Benzoic acid (BA)	121	77	2.52	50	-10	-14	-5	5 – 1000	0.988	50.00	109.79	39.08
										400.00	99.08	8.53
										800.00	93.91	10.20
3-Hydroxybenzoic acid (3OH-BA)	136.7	93	1.8	50	-55	-16	-5	5 – 1000	0.996	50.00	88.42	9.22
										400.00	97.53	4.65
										800.00	98.33	5.34
4-Hydroxybenzoic acid (4OH-BA)	136.7	93.1	1.47	50	-55	-20	-9	5 – 1000	0.995	50.00	87.85	4.90
										400.00	95.99	2.13
										800.00	109.98	7.28
Phenylacetic acid derivatives												
Phenylacetic acid (PAA)	134.8	91.1	2.58	50	-45	-10	-13	25 – 5000	0.998	250.00	101.89	12.93
										2000.00	99.27	2.89
										4000.00	93.18	7.00
3-Hydroxyphenylacetic acid (3OH-PAA)	150.8	107	1.88	50	-45	-12	-5	25 – 5000	0.998	250.00	101.45	5.38
										2000.00	99.07	1.20
										4000.00	93.75	6.02
4-Hydroxyphenylacetic acid (4OH-PAA)	150.8	107	1.66	50	-45	-10	-9	25 – 5000	0.995	250.00	106.01	11.41
										2000.00	96.82	5.96
										4000.00	95.18	7.79
Phenylpropanoate derivatives												
3-Phenylpropanoate acid (PPA)	148.8	105	2.98	50	-55	-14	-9	25 – 5000	0.997	250.00	99.43	6.39
										2000.00	97.27	2.84
										4000.00	94.02	8.29
3-(3-Hydroxyphenyl)-propanoic acid (3OH-PPA)	164.7	106	2.27	50	-65	-30	-15	5 – 1000	0.995	50.00	98.40	17.09
										400.00	98.66	2.23
										800.00	97.95	8.59
3-(4-Hydroxyphenyl)-propanoic acid (4OH-PPA)	164.7	59	2.1	50	-60	-16	-7	5 – 1000	0.996	50.00	107.23	16.38
										400.00	99.99	5.16
										800.00	95.36	7.61
Hippuric acid derivatives												
Hippuric acid (HA)	177.7	134	1.56	50	-50	-16	-11	25 – 5000	0.993	250.00	95.69	18.54
										2000.00	100.92	3.31
										4000.00	96.68	11.88
3-Hydroxyhippuric acid (3OH-HA)	193.7	149.9	0.97	50	-70	-18	-11	5 – 1000	0.996	50.00	95.07	7.54
										400.00	94.43	5.59
										800.00	92.93	9.88
4-Hydroxyhippuric acid (4OH-HA)	193.8	99.9	0.85	50	-50	-14	-9	5 – 1000	0.995	50.00	77.08	12.81
										400.00	91.89	3.94
										800.00	97.45	7.78
Cinnamic acid derivatives												
Cinnamic acid (CNA)	146.7	103	2.99	50	-40	-14	-9	5 – 1000	0.998	50.00	100.33	7.10
										400.00	98.08	6.55
										800.00	94.42	5.91

Table S3. Comparison of various nutrikinetic models with the Akaike information criterion. Akaike information criterion is a measure of relative quality of statistical models between a set of model parameters, with low value denoting better model fit within each weighting (1/Y, 1/Y², no weighting). K_a, 1st order absorption rate constant; K_e, 1st order elimination rate constant; N.A., not applicable.

Weighting	Compartment	Rate constant	Lag time	Elimination rate	AIC value		
					Dose 0	Dose 1	Dose 2
1/Y ²	1	-	No	1 st order	29.58	51.88	10.50
1/Y ²	1	-	Yes	1 st order	31.54	53.82	12.48
1/Y ²	1	K _e =K _a	No	1 st order	32.85	50.23	8.51
1/Y ²	1	K _e =K _a	Yes	1 st order	N.A.	52.23	10.51
1/Y ²	2	Micro	No	1 st order	N.A.	55.12	14.50
1/Y ²	2	Micro	Yes	1 st order	N.A.	57.07	16.47
1/Y	1	-	No	1 st order	26.66	77.05	76.55
1/Y	1	-	Yes	1 st order	28.58	75.98	77.66
1/Y	1	K _e =K _a	No	1 st order	31.30	75.24	74.55
1/Y	1	K _e =K _a	Yes	1 st order	33.30	77.24	76.55
1/Y	2	Micro	No	1 st order	N.A.	N.A.	80.55
1/Y	2	Micro	Yes	1 st order	N.A.	80.02	81.66
No weighting	1	-	No	1 st order	23.66	100.83	127.14
No weighting	1	-	Yes	1 st order	25.54	97.82	124.51
No weighting	1	K _e =K _a	No	1 st order	29.89	106.52	127.45
No weighting	1	K _e =K _a	Yes	1 st order	N.A.	N.A.	N.A.
No weighting	2	Micro	No	1 st order	N.A.	104.83	131.13
No weighting	2	Micro	Yes	1 st order	N.A.	101.87	128.50