Supplementary data

Bioprocessing of hempseed (Cannabis sativa L.) food by-products increased nutrient and phytochemical *in vitro* bioavailability during digestion and microbial fermentation

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Table S1: Quantitative profiling of plant metabolites from the hempseed screenings by targeted LC−MS/MS, concentration in mg/kg, as average n=3 determinations ± STD. Where Free fraction compounds are presented in SET A, Alkaline-bound fraction compounds in SET B, Acid-bound fraction presented in SETC and Total compounds in SET D.

SET A compounds name (mg/Kg)	Initial matrix	First bioprocess			Second bioprocess			
					Free fraction			
	Raw	EM_1	BY_1	EM+BY_1	EM_2	EC_2	BY_2	EC+BY_2
benzoic acid	2.39 ± 0.25	4.77 ± 0.69	10.46 ± 1.49	11.98 ± 0.94	3.48 ± 1.52	3.86 ± 0.56	12.83 ± 1.12	13.48 ± 1.28
Salicylic acid	17.80 ± 2.34	30.84 ± 4.50	30.87 ± 4.49	33.13 ± 1.99	31.25 ± 4.68	34.17 ± 0.86	37.30 ± 3.54	34.55 ± 1.77
p-hydroxybenzoic acid	8.38 ± 1.38	18.06 ± 2.03	22.65 ± 4.28	29.47 ± 3.12	15.76 ± 3.51	20.44 ± 2.21	20.89 ± 2.50	20.26 ± 1.47
2, 3-dihydroxybenzoic acid	nd	nd	nd	nd	0.63 ± 0.04	0.74 ± 0.18	0.68 ± 0.09	0.58 ± 0.06
2, 4-dihydroxybenzoic acid	nd	nd	nd	nd	nd	nd	nd	nd
gentisic acid	nd	nd	nd	nd	1.60 ± 1.13	4.59 ± 1.01	4.18 ± 2.59	7.53 ± 3.96
2, 6-dihydroxybenzoic acid	0.06 ± 0.01	0.12 ± 0.02	0.12 ± 0.03	0.12 ± 0.00	0.30 ± 0.02	0.34 ± 0.02	0.31 ± 0.03	0.28 ± 0.02
protocatechuic acid	7.74 ± 0.73	3.59 ± 0.82	4.65 ± 0.59	4.32 ± 0.65	5.53 ± 0.70	6.22 ± 0.21	6.97 ± 0.82	6.02 ± 0.52

2-methoxybenzoic acid	nd	nd	nd	nd	nd	nd	nd	nd
4-methoxybenzoic acid	nd	nd	nd	nd	nd	nd	nd	nd
3, 4, 5-trihydroxybenzoic acid	nd	nd	nd	nd	0.36 ± 0.03	nd	0.42 ± 0.04	0.49 ± 0.07
Vanillic acid	2.15 ± 0.49	8.32 ± 1.12	9.36 ± 1.87	10.92 ± 0.68	5.80 ± 1.35	6.98 ± 0.51	7.61 ± 0.92	7.03 ± 0.25
3, 5-dimethoxy-4-hydroxybenzoic acid	0.42 ± 0.10	1.17 ± 0.30	1.33 ± 0.32	1.33 ± 0.23	0.84 ± 0.17	1.04 ± 0.04	1.09 ± 0.16	1.04 ± 0.11
p-Hydroxybenzaldehyde	5.80 ± 0.58	9.08 ± 0.93	3.80 ± 1.14	3.32 ± 0.18	8.85 ± 1.40	8.65 ± 1.55	9.15 ± 0.54	8.49 ± 0.78
protocatechualdehyde	4.26 ± 0.82	2.11 ± 0.29	2.28 ± 0.44	2.60 ± 0.17	3.60 ± 0.56	3.82 ± 0.56	4.23 ± 0.38	4.15 ± 0.41
3, 4, 5--trihydroxybenzaldehyde	nd	nd	nd	nd	nd	nd	nd	nd
vanillin	2.20 ± 0.13	3.72 ± 0.73	1.58 ± 0.27	1.46 ± 0.14	3.48 ± 0.53	3.46 ± 0.69	3.31 ± 0.08	3.18 ± 0.34
3, 5-dimethoxy-4-hydroxybenzaldehyde	0.48 ± 0.33	1.35 ± 0.28	1.10 ± 0.29	1.20 ± 0.10	1.19 ± 0.23	1.26 ± 0.08	1.29 ± 0.14	1.31 ± 0.09
cinnamic acid	0.19 ± 0.04	0.26 ± 0.03	0.32 ± 0.01	0.27 ± 0.05	0.49 ± 0.08	0.51 ± 0.04	0.54 ± 0.05	0.51 ± 0.05
p-Coumaric acid	1.22 ± 0.16	0.65 ± 0.13	0.81 ± 0.11	1.32 ± 0.13	2.44 ± 0.50	3.08 ± 0.37	3.33 ± 0.38	3.75 ± 0.28
caffeic acid	0.09 ± 0.04	0.73 ± 0.21	0.85 ± 0.11	1.10 ± 0.05	3.03 ± 0.59	3.55 ± 1.23	3.54 ± 0.39	4.01 ± 0.17
ferulic acid	0.99 ± 0.11	14.57 ± 2.68	20.52 ± 3.32	19.37 ± 0.83	23.91 ± 5.70	30.89 ± 1.64	35.41 ± 3.62	33.46 ± 1.62
3, 5-dimethoxy-4-hydroxycinnamic acid	nd	nd	nd	nd	nd	nd	nd	nd
3-hydroxyphenylpropionic acid	0.55 ± 0.11	0.88 ± 0.16	0.77 ± 0.13	0.96 ± 0.07	1.08 ± 0.29	1.33 ± 0.03	1.38 ± 0.16	1.28 ± 0.01
Phloretic acid	1.53 ± 0.35	nd	nd	2.42 ± 0.30	3.90 ± 1.03	5.04 ± 0.38	5.10 ± 0.72	4.86 ± 0.44
3-methoxy-4-hydroxyphenylpropionic acid	nd	0.22 ± 0.02	0.23 ± 0.08	0.30 ± 0.07	0.28 ± 0.07	0.37 ± 0.03	0.32 ± 0.01	0.37 ± 0.03
4-hydroxyacetophenone	0.01 ± 0.00	0.05 ± 0.02	0.06 ± 0.02	0.07 ± 0.01	0.11 ± 0.00	0.12 ± 0.01	0.12 ± 0.01	0.11 ± 0.00
3-methoxy-4-hydroxyacetophenone	nd	0.09 ± 0.01	0.11 ± 0.03	0.11 ± 0.02	0.15 ± 0.02	0.14 ± 0.00	0.14 ± 0.01	0.13 ± 0.01

3, 5-dimethoxy-4-hydroxyacetophenone	nd	nd	nd	nd	nd	0.08 ± 0.07	nd	nd
phenylacetic acid	0.24 ± 0.02	0.66 ± 0.15	5.22 ± 0.74	5.57 ± 0.23	nd	nd	nd	nd
4-hydroxyphenylacetic acid	nd	nd	nd	nd	nd	nd	2.24 ± 0.30	2.90 ± 0.14
3, 4-dihydroxyphenylacetic acid (Homoprotocatechuic acid)	nd	nd	nd	nd	6.35 ± 1.58	7.82 ± 0.52	8.67 ± 0.83	7.91 ± 0.70
indole-3-acetic acid	nd	nd	nd	0.12 ± 0.01	0.20 ± 0.02	0.21 ± 0.01	0.33 ± 0.03	0.30 ± 0.02
indole-3-carboxylic acid	0.46 ± 0.04	1.02 ± 0.41	1.02 ± 0.05	1.28 ± 0.20	1.56 ± 0.33	1.66 ± 0.18	1.86 ± 0.07	1.67 ± 0.17
indole-4-propionic acid	nd	nd	nd	nd	0.14 ± 0.01	0.14 ± 0.01	0.14 ± 0.01	nd
Chlorogenic acid	0.07 ± 0.12	nd	nd	nd	0.51 ± 0.01	0.50 ± 0.16	0.46 ± 0.02	0.35 ± 0.02
3-hydroxymandelic acid	nd	nd	nd	nd	nd	nd	nd	nd
3, 4-dihydroxymandelic acid	0.31 ± 0.06	0.13 ± 0.11	nd	0.06 ± 0.06	nd	nd	nd	nd
4-hydroxy-3-methoxy-mandelic acid	nd	nd	nd	nd	nd	nd	nd	nd
phenyllactic acid	nd	0.05 ± 0.02	0.83 ± 0.12	0.99 ± 0.08	nd	nd	0.27 ± 0.06	0.26 ± 0.03
4-hydroxyphenyllactic acid	nd	nd	nd	nd	nd	nd	0.48 ± 0.03	0.40 ± 0.07
phenylpyruvic acid	nd	nd	0.52 ± 0.11	0.71 ± 0.09	0.13 ± 0.05	0.13 ± 0.11	0.17 ± 0.06	0.25 ± 0.02
ethylferulate	nd	nd	nd	nd	0.21 ± 0.02	0.20 ± 0.02	0.20 ± 0.01	0.20 ± 0.00
catechin	nd	nd	nd	nd	nd	nd	nd	nd
epicatechin	nd	nd	nd	nd	nd	nd	nd	nd
gallocatechin	nd	nd	nd	nd	nd	nd	nd	nd
epigallocatechin	nd	nd	nd	nd	nd	nd	nd	nd

isoliquiritigenin	0.08 ± 0.00	nd	nd	nd	nd	nd	nd	nd
naringenin	nd	nd	0.00 ± 0.01	0.01 ± 0.00	nd	nd	nd	nd
kaempferol	nd	nd	nd	nd	nd	nd	nd	nd
quercetin	nd	nd	0.13 ± 0.12	0.06 ± 0.10	nd	0.14 ± 0.13	0.11 ± 0.10	0.18 ± 0.06
quercetin-3-glucoside	0.40 ± 0.03	0.25 ± 0.04	0.26 ± 0.03	0.23 ± 0.02	0.12 ± 0.03	0.08 ± 0.03	0.09 ± 0.01	0.09 ± 0.01
taxifolin	nd	nd	nd	nd	0.20 ± 0.08	0.24 ± 0.06	0.28 ± 0.03	0.26 ± 0.00
biochanin a	0.08 ± 0.01	0.43 ± 0.02	0.40 ± 0.09	0.47 ± 0.03	nd	nd	nd	nd
luteolin	0.47 ± 0.05	2.97 ± 0.54	3.06 ± 0.74	3.57 ± 0.22	2.64 ± 0.82	2.91 ± 1.14	3.38 ± 0.43	3.21 ± 0.71
apigenin	0.14 ± 0.01	0.96 ± 0.11	0.79 ± 0.13	1.00 ± 0.16	1.02 ± 0.28	1.15 ± 0.19	1.03 ± 0.09	1.19 ± 0.17
tyrosol	nd	nd	nd	nd	nd	nd	nd	nd
hydroxytyrosol	nd	0.01 ± 0.00	0.01 ± 0.01	0.01 ± 0.00	nd	nd	0.02 ± 0.01	0.04 ± 0.01
isorhamnetin	nd	0.22 ± 0.04	0.30 ± 0.07	0.28 ± 0.01	0.11 ± 0.09	0.26 ± 0.24	0.31 ± 0.07	0.37 ± 0.09
rutin	0.21 ± 0.01	nd	nd	nd	nd	nd	nd	nd
vitexin	0.07 ± 0.01	0.13 ± 0.04	0.16 ± 0.10	0.15 ± 0.01	0.26 ± 0.19	0.16 ± 0.04	0.16 ± 0.01	0.14 ± 0.02
isovitexin	0.07 ± 0.01	0.13 ± 0.04	0.16 ± 0.10	0.15 ± 0.01	0.25 ± 0.20	0.15 ± 0.04	0.15 ± 0.01	0.10 ± 0.09
hyperoside	0.45 ± 0.09	0.24 ± 0.06	0.25 ± 0.05	0.20 ± 0.01	0.14 ± 0.03	0.10 ± 0.03	0.10 ± 0.00	0.10 ± 0.01
hesperitin	nd	nd	nd	nd	nd	nd	nd	0.01 ± 0.00
ferulic dimer 8-5c	nd	nd	nd	nd	nd	nd	nd	nd
secoisolariciresinol	nd	nd	nd	nd	nd	nd	nd	nd
syringaresinol	nd	nd	nd	nd	nd	nd	nd	nd

pinoresinol	nd	0.67 ± 0.09	0.67 ± 0.19	0.66 ± 0.12	0.49 ± 0.11	0.57 ± 0.06	0.79 ± 0.03	0.72 ± 0.06

SET B compounds name (mg/Kg)	**Initial matrix**	**First bioprocess**			**Second bioprocess**			
		Alkaline-bound fraction						
	Raw	**EM_1**	**BY_1**	**EM+BY_1**	**EM_2**	**EC_2**	**BY_2**	**EC+BY_2**
benzoic acid	1.54 ± 0.57	1.21 ± 0.20	0.97 ± 0.84	1.30 ± 0.48	0.99 ± 0.26	1.66 ± 0.26	1.58 ± 0.49	0.93 ± 0.61
Salicylic acid	5.53 ± 1.84	1.58 ± 0.09	1.49 ± 0.48	1.74 ± 0.22	3.43 ± 0.61	3.85 ± 0.39	3.92 ± 0.26	3.11 ± 0.65
p-hydroxybenzoic acid	8.23 ± 2.10	3.65 ± 0.22	3.71 ± 1.01	4.42 ± 0.78	6.65 ± 0.46	6.50 ± 0.32	7.11 ± 1.23	5.64 ± 1.05
2, 3-dihydroxybenzoic acid	nd	nd	nd	nd	0.24 ± 0.01	0.29 ± 0.01	0.24 ± 0.01	0.24 ± 0.01
2, 4-dihydroxybenzoic acid	nd	nd	nd	nd	0.66 ± 0.03	0.52 ± 0.04	0.19 ± 0.32	0.35 ± 0.30
gentisic acid	nd	nd	nd	nd	0.54 ± 0.09	0.85 ± 0.03	0.68 ± 0.07	0.59 ± 0.05
2, 6-dihydroxybenzoic acid	0.03 ± 0.02	0.03 ± 0.00	0.04 ± 0.02	0.04 ± 0.01	nd	nd	nd	nd
protocatechuic acid	22.53 ± 7.34	15.21 ± 1.32	15.65 ± 4.54	19.03 ± 2.20	32.79 ± 2.61	29.09 ± 2.28	34.47 ± 1.97	27.27 ± 2.74
2-methoxybenzoic acid	nd	nd	nd	nd	nd	nd	nd	nd
4-methoxybenzoic acid	nd	nd	nd	nd	1.05 ± 0.09	0.54 ± 0.06	0.97 ± 0.11	0.67 ± 0.36
3, 4, 5-trihydroxybenzoic acid	0.09 ± 0.06	nd	nd	nd	nd	0.25 ± 0.02	0.22 ± 0.03	nd
Vanillic acid	3.83 ± 0.94	3.19 ± 0.10	3.09 ± 0.92	3.40 ± 0.63	6.27 ± 0.38	6.36 ± 0.34	6.84 ± 0.96	5.54 ± 0.76
3, 5-dimethoxy-4-hydroxybenzoic acid	1.02 ± 0.17	0.68 ± 0.08	0.61 ± 0.26	0.67 ± 0.10	1.56 ± 0.16	1.55 ± 0.11	1.62 ± 0.17	1.35 ± 0.18
p-Hydroxybenzaldehyde	6.64 ± 1.28	4.25 ± 0.34	4.31 ± 0.93	4.98 ± 0.43	6.76 ± 0.17	6.24 ± 0.03	7.15 ± 1.08	5.94 ± 0.81

protocatechualdehyde	32.97 ± 5.62	19.42 ± 1.66	19.33 ± 3.53	22.23 ± 2.92	29.54 ± 1.36	26.48 ± 0.95	29.85 ± 3.36	27.10 ± 2.07
3, 4, 5--trihydroxybenzaldehyde	nd	nd	nd	nd	2.03 ± 2.78	0.37 ± 0.03	0.37 ± 0.02	0.44 ± 0.18
vanillin	9.37 ± 0.93	7.52 ± 0.61	7.91 ± 2.04	8.58 ± 0.33	14.85 ± 1.13	14.92 ± 0.53	16.46 ± 2.21	13.77 ± 1.71
3, 5-dimethoxy-4-hydroxybenzaldehyde	3.94 ± 0.49	2.70 ± 0.36	2.71 ± 0.62	2.77 ± 0.29	7.29 ± 0.15	6.88 ± 0.26	7.63 ± 0.86	6.51 ± 0.70
cinnamic acid	0.06 ± 0.02	0.07 ± 0.03	0.08 ± 0.03	0.10 ± 0.02	0.27 ± 0.05	0.27 ± 0.02	0.31 ± 0.03	0.23 ± 0.04
p-Coumaric acid	45.76 ± 11.22	36.25 ± 2.46	33.78 ± 7.18	37.65 ± 6.19	75.51 ± 5.56	79.18 ± 2.87	80.49 ± 8.65	69.27 ± 10.43
caffeic acid	0.98 ± 0.50	1.46 ± 0.20	1.22 ± 0.37	1.32 ± 0.15	2.83 ± 0.27	3.51 ± 0.03	3.24 ± 0.36	2.64 ± 0.47
ferulic acid	5.64 ± 1.23	2.97 ± 0.29	3.00 ± 0.69	3.31 ± 0.37	6.25 ± 0.53	6.75 ± 0.26	6.58 ± 0.88	6.05 ± 1.29
3, 5-dimethoxy-4-hydroxycinnamic acid	nd	nd	nd	nd	0.33 ± 0.02	0.37 ± 0.01	0.39 ± 0.01	0.36 ± 0.03
3-hydroxyphenylpropionic acid	0.72 ± 0.18	0.50 ± 0.04	0.61 ± 0.10	0.65 ± 0.08	nd	nd	nd	nd
Phloretic acid	1.61 ± 0.20	nd	nd	nd	5.41 ± 0.52	5.59 ± 0.19	6.26 ± 0.84	4.98 ± 1.16
3-methoxy-4-hydroxyphenylpropionic acid	nd	nd	nd	nd	nd	nd	nd	nd
4-hydroxyacetophenone	0.08 ± 0.01	0.07 ± 0.01	0.05 ± 0.02	0.07 ± 0.02	0.13 ± 0.01	0.13 ± 0.01	0.13 ± 0.01	0.12 ± 0.01
3-methoxy-4-hydroxyacetophenone	0.07 ± 0.02	0.07 ± 0.01	0.05 ± 0.05	0.06 ± 0.05	0.22 ± 0.02	0.22 ± 0.02	0.24 ± 0.04	0.21 ± 0.02
3, 5-dimethoxy-4-hydroxyacetophenone	nd	nd	nd	nd	0.19 ± 0.01	0.21 ± 0.01	0.23 ± 0.03	0.20 ± 0.03
phenylacetic acid	0.07 ± 0.00	0.15 ± 0.06	0.12 ± 0.02	0.18 ± 0.05	nd	nd	nd	nd
4-hydroxyphenylacetic acid	nd	nd	nd	nd	nd	nd	nd	nd
3, 4-dihydroxyphenylacetic acid (Homoprotocatechuic acid)	nd	nd	nd	nd	4.71 ± 0.28	4.91 ± 0.36	5.35 ± 0.81	4.35 ± 0.62
indole-3-acetic acid	0.08 ± 0.04	nd	nd	nd	0.17 ± 0.00	0.16 ± 0.01	0.17 ± 0.01	0.16 ± 0.01
indole-3-carboxylic acid	0.81 ± 0.30	0.35 ± 0.02	0.30 ± 0.09	0.39 ± 0.05	0.82 ± 0.08	0.84 ± 0.06	0.85 ± 0.09	0.77 ± 0.11
indole-4-propionic acid	nd	nd	nd	nd	nd	nd	nd	nd
Chlorogenic acid	nd	nd	nd	nd	0.12 ± 0.10	0.19 ± 0.01	0.11 ± 0.10	nd
3-hydroxymandelic acid	1.49 ± 0.94	2.32 ± 0.27	1.44 ± 0.25	1.94 ± 0.25	nd	nd	nd	nd
3, 4-dihydroxymandelic acid	0.32 ± 0.13	0.27 ± 0.17	0.14 ± 0.21	0.27 ± 0.17	nd	nd	nd	nd
4-hydroxy-3-methoxy-mandelic acid	nd	nd	nd	nd	nd	nd	nd	nd
phenyllactic acid	nd	nd	nd	nd	nd	nd	nd	nd

4-hydroxyphenyllactic acid	1.20 ± 0.46	nd	nd	nd	nd	nd	nd	nd
phenylpyruvic acid	nd	0.38 ± 0.06	0.37 ± 0.08	0.48 ± 0.05	0.74 ± 0.01	0.89 ± 0.24	0.67 ± 0.14	0.71 ± 0.22
ethylferulate	nd	nd	nd	nd	nd	nd	nd	nd
catechin	1.72 ± 1.49	2.63 ± 1.06	5.57 ± 2.65	3.91 ± 2.37	3.35 ± 1.72	10.61 ± 2.23	9.63 ± 2.35	6.26 ± 1.20
epicatechin	nd	nd	nd	nd	0.18 ± 0.32	1.35 ± 0.42	1.06 ± 0.26	0.80 ± 0.25
gallocatechin	nd	0.90 ± 0.22	0.83 ± 0.60	0.64 ± 0.27	0.20 ± 0.04	0.52 ± 0.27	0.65 ± 0.36	0.25 ± 0.07
epigallocatechin	nd	0.35 ± 0.07	0.22 ± 0.08	0.25 ± 0.12	nd	nd	nd	nd
isoliquiritigenin	nd	nd	nd	nd	nd	nd	nd	nd
naringenin	nd	nd	nd	nd	nd	nd	nd	nd
kaempferol	nd	nd	nd	nd	nd	0.15 ± 0.00	0.16 ± 0.01	0.13 ± 0.02
quercetin	0.42 ± 0.20	0.90 ± 0.20	1.03 ± 0.24	1.15 ± 0.28	0.88 ± 0.07	1.13 ± 0.09	1.08 ± 0.39	0.87 ± 0.16
quercetin-3-glucoside	0.15 ± 0.03	0.10 ± 0.03	0.08 ± 0.02	0.09 ± 0.03	0.07 ± 0.00	0.10 ± 0.02	0.09 ± 0.01	0.07 ± 0.02
taxifolin	0.20 ± 0.19	0.36 ± 0.08	0.36 ± 0.08	0.35 ± 0.11	0.41 ± 0.07	0.67 ± 0.05	0.74 ± 0.10	0.46 ± 0.11
biochanin a	nd	nd	nd	nd	nd	nd	nd	nd
luteolin	0.30 ± 0.08	0.37 ± 0.07	0.34 ± 0.07	0.38 ± 0.05	0.51 ± 0.02	0.55 ± 0.08	0.58 ± 0.06	0.48 ± 0.09
apigenin	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.01	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.01
tyrosol	0.02 ± 0.03	nd	nd	nd	nd	nd	nd	nd
hydroxytyrosol	0.12 ± 0.03	0.07 ± 0.04	0.07 ± 0.06	0.06 ± 0.04	nd	nd	nd	nd
isorhamnetin	0.22 ± 0.03	0.32 ± 0.04	0.29 ± 0.03	0.29 ± 0.03	0.30 ± 0.01	0.37 ± 0.04	0.33 ± 0.05	0.30 ± 0.03
rutin	nd	nd	nd	nd	nd	0.04 ± 0.07	nd	nd
vitexin	nd	nd	nd	nd	0.03 ± 0.05	0.04 ± 0.06	nd	0.04 ± 0.07
isovitexin	nd	nd	nd	nd	nd	nd	nd	nd
hyperoside	0.13 ± 0.02	0.08 ± 0.02	0.06 ± 0.01	0.07 ± 0.03	0.08 ± 0.01	0.10 ± 0.02	0.09 ± 0.01	0.07 ± 0.01
hesperitin	nd	nd	nd	nd	nd	nd	nd	nd
ferulic dimer 8-5c	nd	0.49 ± 0.06	0.30 ± 0.06	0.36 ± 0.04	nd	nd	nd	nd
secoisolariciresinol	0.21 ± 0.07	0.22 ± 0.01	0.18 ± 0.04	0.23 ± 0.06	0.20 ± 0.01	0.13 ± 0.01	0.19 ± 0.07	0.16 ± 0.09
syringaresinol	nd	nd	nd	nd	1.12 ± 1.93	2.81 ± 2.43	1.24 ± 2.15	2.27 ± 1.97
pinoresinol	nd	nd	nd	nd	0.18 ± 0.00	0.18 ± 0.02	0.17 ± 0.01	0.17 ± 0.04

SET C compounds name (mg/Kg)	Initial matrix	First bioprocess			Second bioprocess			
	Acid-bound fraction							
	Raw	EM_1	BY_1	EM+BY_1	EM_2	EC_2	BY_2	EC+BY_2
benzoic acid	1.83 ± 0.40	1.28 ± 0.08	1.04 ± 0.49	0.74 ± 0.16	0.69 ± 0.34	0.59 ± 0.10	0.78 ± 0.25	0.67 ± 0.38
Salicylic acid	2.26 ± 0.10	1.82 ± 0.25	1.77 ± 0.05	1.85 ± 0.46	2.06 ± 0.30	2.02 ± 0.14	1.91 ± 0.20	2.03 ± 0.33
p-hydroxybenzoic acid	6.51 ± 0.55	5.02 ± 0.43	5.86 ± 0.49	5.37 ± 0.99	5.52 ± 0.67	5.06 ± 0.40	5.78 ± 0.74	5.25 ± 0.72
2, 3-dihydroxybenzoic acid	nd	nd	nd	nd	0.32 ± 0.02	0.30 ± 0.01	0.30 ± 0.01	0.30 ± 0.01
2, 4-dihydroxybenzoic acid	nd	nd	nd	nd	nd	nd	nd	nd
gentisic acid	nd	nd	nd	nd	32.56 ± 3.91	24.98 ± 1.66	33.48 ± 4.28	24.37 ± 2.40
2, 6-dihydroxybenzoic acid	nd	nd	nd	nd	nd	nd	nd	nd
protocatechuic acid	13.38 ± 1.03	13.29 ± 1.03	16.37 ± 1.70	16.84 ± 2.16	17.93 ± 1.47	13.70 ± 1.25	16.83 ± 1.06	16.15 ± 0.47
2-methoxybenzoic acid	3.39 ± 0.83	nd	nd	nd	nd	nd	nd	nd
4-methoxybenzoic acid	nd	nd	nd	nd	nd	nd	nd	nd
3, 4, 5-trihydroxybenzoic acid	0.21 ± 0.13	0.24 ± 0.10	0.17 ± 0.07	0.22 ± 0.09	0.28 ± 0.02	0.30 ± 0.02	0.28 ± 0.01	0.29 ± 0.03
Vanillic acid	8.99 ± 1.55	8.40 ± 0.54	8.63 ± 0.46	8.48 ± 1.50	10.70 ± 1.49	8.33 ± 1.25	9.84 ± 0.74	9.45 ± 0.30
3, 5-dimethoxy-4-hydroxybenzoic acid	3.78 ± 0.70	3.70 ± 0.59	3.74 ± 0.36	3.98 ± 0.75	7.36 ± 1.16	5.32 ± 1.37	6.59 ± 0.45	6.47 ± 0.29
p-Hydroxybenzaldehyde	1.78 ± 0.26	1.45 ± 0.18	1.53 ± 0.09	1.59 ± 0.30	2.53 ± 0.28	1.69 ± 0.31	2.09 ± 0.08	2.20 ± 0.24
protocatechualdehyde	7.01 ± 1.15	7.28 ± 1.05	7.48 ± 0.31	7.50 ± 1.07	8.61 ± 0.77	7.08 ± 0.75	7.94 ± 0.30	7.18 ± 0.21
3, 4, 5--trihydroxybenzaldehyde	nd	nd	nd	nd	nd	nd	nd	nd
vanillin	5.11 ± 0.70	5.11 ± 0.64	4.79 ± 0.48	4.83 ± 0.81	9.37 ± 1.05	7.38 ± 1.41	7.65 ± 0.49	8.05 ± 0.60
3, 5-dimethoxy-4-hydroxybenzaldehyde	6.20 ± 0.85	6.22 ± 0.63	6.64 ± 0.75	6.47 ± 0.80	15.83 ± 1.96	11.52 ± 2.28	13.24 ± 0.72	13.51 ± 0.62
cinnamic acid	0.09 ± 0.02	0.10 ± 0.02	0.08 ± 0.00	0.09 ± 0.03	0.19 ± 0.01	0.16 ± 0.01	0.17 ± 0.02	0.18 ± 0.02
p-Coumaric acid	6.72 ± 0.81	6.67 ± 0.41	7.01 ± 0.78	6.69 ± 1.04	7.99 ± 1.34	6.83 ± 1.03	6.91 ± 0.73	6.81 ± 0.51
caffeic acid	0.97 ± 0.05	0.83 ± 0.15	0.85 ± 0.01	0.86 ± 0.12	0.90 ± 0.10	0.88 ± 0.13	0.92 ± 0.13	0.85 ± 0.05
ferulic acid	9.67 ± 1.42	8.96 ± 1.06	9.08 ± 0.61	9.21 ± 0.81	9.65 ± 1.17	9.94 ± 0.61	10.05 ± 1.33	9.70 ± 0.92
3, 5-dimethoxy-4-hydroxycinnamic acid	0.44 ± 0.07	0.45 ± 0.06	0.49 ± 0.03	0.49 ± 0.05	nd	nd	nd	nd
3-hydroxyphenylpropionic acid	nd	nd	nd	nd	nd	nd	nd	nd
Phloretic acid	nd	nd	nd	nd	nd	nd	nd	nd

3-methoxy-4-hydroxyphenylpropionic acid	0.90 ± 0.11	0.98 ± 0.17	0.98 ± 0.12	0.95 ± 0.22	0.90 ± 0.15	0.88 ± 0.07	0.97 ± 0.15	0.89 ± 0.10
4-hydroxyacetophenone	0.12 ± 0.02	0.09 ± 0.01	0.07 ± 0.01	0.08 ± 0.02	0.14 ± 0.01	0.11 ± 0.01	0.13 ± 0.01	0.13 ± 0.01
3-methoxy-4-hydroxyacetophenone	0.39 ± 0.03	0.35 ± 0.03	0.34 ± 0.03	0.35 ± 0.02	0.49 ± 0.04	0.41 ± 0.05	0.47 ± 0.04	0.52 ± 0.03
3, 5-dimethoxy-4-hydroxyacetophenone	nd	nd	nd	nd	0.58 ± 0.09	0.44 ± 0.08	0.52 ± 0.05	0.51 ± 0.02
phenylacetic acid	nd	nd	nd	nd	nd	nd	nd	nd
4-hydroxyphenylacetic acid	nd	nd	nd	nd	nd	nd	2.27 ± 0.26	2.62 ± 0.28
3, 4-dihydroxyphenylacetic acid (Homoprotocatechuic acid)	nd	nd	nd	nd	8.73 ± 1.21	7.55 ± 1.15	8.05 ± 0.87	8.05 ± 0.57
indole-3-acetic acid	nd	nd	nd	nd	nd	nd	nd	nd
indole-3-carboxylic acid	nd	nd	nd	nd	nd	nd	nd	nd
indole-4-propionic acid	nd	nd	nd	nd	nd	nd	nd	nd
Chlorogenic acid	nd	nd	nd	nd	nd	nd	nd	nd
3-hydroxymandelic acid	2.48 ± 0.57	2.71 ± 0.12	3.04 ± 0.27	2.93 ± 0.44	nd	nd	nd	nd
3, 4-dihydroxymandelic acid	nd	nd	0.11 ± 0.10	0.06 ± 0.11	nd	nd	nd	nd
4-hydroxy-3-methoxy-mandelic acid	0.97 ± 0.09	0.86 ± 0.19	nd	nd	nd	nd	nd	nd
phenyllactic acid	nd	nd	nd	nd	nd	nd	nd	nd
4-hydroxyphenyllactic acid	nd	nd	nd	nd	0.56 ± 0.15	0.50 ± 0.04	0.54 ± 0.03	0.53 ± 0.08
phenylpyruvic acid	nd	0.35 ± 0.02	0.34 ± 0.01	0.39 ± 0.03	1.77 ± 0.22	1.09 ± 0.06	1.77 ± 0.23	2.25 ± 0.21
ethylferulate	nd	nd	nd	nd	nd	nd	nd	nd
catechin	nd	nd	nd	0.04 ± 0.06	nd	nd	nd	nd
epicatechin	nd	nd	nd	nd	nd	nd	nd	nd
gallocatechin	nd	nd	nd	nd	nd	nd	nd	nd
epigallocatechin	nd	nd	nd	nd	nd	nd	nd	nd
isoliquiritigenin	nd	nd	nd	nd	nd	nd	nd	nd
naringenin	nd	nd	nd	nd	nd	nd	nd	nd
kaempferol	nd	nd	nd	nd	nd	nd	nd	nd
quercetin	0.07 ± 0.11	0.29 ± 0.03	0.28 ± 0.06	0.27 ± 0.02	0.08 ± 0.07	0.15 ± 0.02	0.15 ± 0.03	0.12 ± 0.00

quercetin-3-glucoside	nd	nd	nd	nd	nd	nd	nd	nd
taxifolin	0.10 ± 0.09	0.06 ± 0.10	0.11 ± 0.09	0.14 ± 0.01	nd	0.05 ± 0.01	0.05 ± 0.02	nd
biochanin a	0.07 ± 0.01	0.04 ± 0.04	0.07 ± 0.00	0.07 ± 0.01	nd	nd	nd	nd
luteolin	0.58 ± 0.14	0.37 ± 0.06	0.41 ± 0.08	0.47 ± 0.13	0.20 ± 0.01	0.21 ± 0.02	0.20 ± 0.01	0.20 ± 0.01
apigenin	0.17 ± 0.03	0.13 ± 0.02	0.13 ± 0.02	0.14 ± 0.01	0.08 ± 0.00	0.08 ± 0.00	0.08 ± 0.00	0.08 ± 0.00
tyrosol	nd	nd	nd	nd	nd	nd	nd	nd
hydroxytyrosol	0.06 ± 0.00	0.06 ± 0.02	0.08 ± 0.01	0.10 ± 0.04	nd	nd	nd	nd
isorhamnetin	nd	nd	0.19 ± 0.01	0.17 ± 0.01	nd	nd	nd	nd
rutin	nd	nd	nd	nd	nd	nd	nd	nd
vitexin	0.23 ± 0.25	0.05 ± 0.01	nd	0.05 ± 0.00	0.04 ± 0.04	0.05 ± 0.04	0.04 ± 0.04	0.04 ± 0.04
isovitexin	0.23 ± 0.25	0.05 ± 0.01	nd	0.05 ± 0.00	nd	0.02 ± 0.04	nd	nd
hyperoside	nd	nd	nd	nd	nd	nd	nd	nd
hesperitin	nd	nd	nd	nd	nd	nd	nd	nd
ferulic dimer 8-5c	nd	nd	nd	nd	0.01 ± 0.01	0.01 ± 0.02	nd	nd
secoisolariciresinol	nd	nd	nd	nd	nd	nd	nd	nd
syringaresinol	72.55 ± 16.63	92.09 ± 16.34	89.99 ± 13.29	95.05 ± 1.11	82.46 ± 10.68	79.72 ± 11.26	73.49 ± 7.69	82.72 ± 3.11
pinoresinol	0.27 ± 0.03	0.37 ± 0.07	0.35 ± 0.04	0.33 ± 0.01	0.17 ± 0.04	0.18 ± 0.04	0.16 ± 0.02	0.16 ± 0.03

SET D compounds name (mg/Kg)	Initial matrix	First bioprocess			Second bioprocess			
	Total content							
	Raw	EM_1	BY_1	EM+BY_1	EM_2	EC_2	BY_2	EC+BY_2
benzoic acid	5.77 ± 0.72	7.26 ± 0.60	12.47 ± 2.54	14.02 ± 0.97	5.16 ± 1.48	6.11 ± 0.85	15.20 ± 1.40	15.08 ± 1.64
Salicylic acid	25.59 ± 4.11	34.24 ± 4.65	34.13 ± 4.87	36.72 ± 2.11	36.74 ± 5.33	40.04 ± 1.11	43.14 ± 3.70	39.70 ± 1.86
p-hydroxybenzoic acid	23.12 ± 2.71	26.73 ± 2.01	32.22 ± 4.46	39.26 ± 2.93	27.92 ± 4.24	32.00 ± 2.01	33.79 ± 3.64	31.15 ± 1.25
2, 3-dihydroxybenzoic acid	nd	nd	nd	nd	1.19 ± 0.05	1.33 ± 0.19	1.23 ± 0.11	1.12 ± 0.06
2, 4-dihydroxybenzoic acid	nd	nd	nd	nd	0.66 ± 0.03	0.52 ± 0.04	0.19 ± 0.32	0.35 ± 0.30
gentisic acid	nd	nd	nd	nd	34.70 ± 5.11	30.41 ± 2.62	38.34 ± 6.90	32.50 ± 5.95
2, 6-dihydroxybenzoic acid	0.10 ± 0.03	0.15 ± 0.02	0.16 ± 0.04	0.16 ± 0.01	0.30 ± 0.02	0.34 ± 0.02	0.31 ± 0.03	0.28 ± 0.02
protocatechuic acid	43.66 ± 7.13	32.09 ± 1.75	36.67 ± 4.27	40.18 ± 4.76	56.25 ± 3.75	49.01 ± 1.85	58.26 ± 3.07	49.44 ± 3.05
2-methoxybenzoic acid	3.39 ± 0.83	nd	nd	nd	nd	nd	nd	nd
4-methoxybenzoic acid	nd	nd	nd	nd	1.05 ± 0.09	0.54 ± 0.06	0.97 ± 0.11	0.67 ± 0.36
3, 4, 5-trihydroxybenzoic acid	0.30 ± 0.19	0.24 ± 0.10	0.17 ± 0.07	0.22 ± 0.09	0.64 ± 0.01	0.55 ± 0.04	0.92 ± 0.05	0.78 ± 0.07
Vanillic acid	14.97 ± 0.93	19.91 ± 1.33	21.08 ± 3.04	22.80 ± 1.53	22.77 ± 2.51	21.67 ± 0.61	24.30 ± 2.10	22.03 ± 0.49
3, 5-dimethoxy-4-hydroxybenzoic acid	5.22 ± 0.49	5.55 ± 0.75	5.68 ± 0.78	5.99 ± 0.93	9.76 ± 1.30	7.91 ± 1.34	9.30 ± 0.59	8.86 ± 0.25
p-Hydroxybenzaldehyde	14.22 ± 1.64	14.77 ± 0.68	9.64 ± 2.04	9.89 ± 0.73	18.13 ± 1.61	16.58 ± 1.84	18.39 ± 1.29	16.63 ± 1.39
protocatechualdehyde	44.24 ± 5.40	28.81 ± 1.90	29.09 ± 3.63	32.33 ± 3.78	41.75 ± 2.31	37.38 ± 1.06	42.02 ± 3.29	38.43 ± 2.04
3, 4, 5--trihydroxybenzaldehyde	nd	nd	nd	nd	2.03 ± 2.78	0.37 ± 0.03	0.37 ± 0.02	0.44 ± 0.18
vanillin	16.67 ± 0.65	16.34 ± 0.73	14.28 ± 2.76	14.87 ± 1.11	27.71 ± 2.08	25.77 ± 2.58	27.42 ± 2.26	24.99 ± 1.29
3, 5-dimethoxy-4-hydroxybenzaldehyde	10.63 ± 0.71	10.27 ± 0.51	10.46 ± 1.52	10.43 ± 1.06	24.31 ± 2.02	19.65 ± 2.58	22.17 ± 1.14	21.32 ± 0.71
cinnamic acid	0.34 ± 0.06	0.43 ± 0.04	0.47 ± 0.04	0.47 ± 0.09	0.95 ± 0.13	0.94 ± 0.06	1.02 ± 0.08	0.92 ± 0.01

p-Coumaric acid	53.71 ± 10.72	43.56 ± 2.39	41.60 ± 7.79	45.66 ± 7.02	85.94 ± 6.68	89.09 ± 4.22	90.73 ± 8.69	79.83 ± 10.05
caffeic acid	2.03 ± 0.49	3.02 ± 0.38	2.93 ± 0.37	3.28 ± 0.31	6.76 ± 0.87	7.93 ± 1.32	7.70 ± 0.76	7.51 ± 0.47
ferulic acid	16.30 ± 0.47	26.51 ± 3.45	32.60 ± 4.16	31.90 ± 1.63	39.81 ± 6.60	47.59 ± 2.27	52.04 ± 5.09	49.22 ± 0.87
3, 5-dimethoxy-4-hydroxycinnamic acid	0.44 ± 0.07	0.45 ± 0.06	0.49 ± 0.03	0.49 ± 0.05	0.33 ± 0.02	0.37 ± 0.01	0.39 ± 0.01	0.36 ± 0.03
3-hydroxyphenylpropionic acid	1.27 ± 0.28	1.38 ± 0.20	1.38 ± 0.21	1.60 ± 0.11	1.08 ± 0.29	1.33 ± 0.03	1.38 ± 0.16	1.28 ± 0.01
Phloretic acid	3.14 ± 0.32	nd	nd	2.42 ± 0.30	9.31 ± 1.43	10.63 ± 0.45	11.36 ± 1.44	9.84 ± 0.75
3-methoxy-4-hydroxyphenylpropionic acid	0.90 ± 0.11	1.20 ± 0.19	1.21 ± 0.09	1.25 ± 0.18	1.19 ± 0.21	1.25 ± 0.05	1.29 ± 0.16	1.27 ± 0.08
4-hydroxyacetophenone	0.20 ± 0.00	0.21 ± 0.02	0.19 ± 0.05	0.22 ± 0.05	0.38 ± 0.01	0.36 ± 0.02	0.38 ± 0.02	0.36 ± 0.01
3-methoxy-4-hydroxyacetophenone	0.46 ± 0.02	0.50 ± 0.04	0.50 ± 0.07	0.52 ± 0.03	0.86 ± 0.04	0.78 ± 0.06	0.85 ± 0.05	0.86 ± 0.03
3, 5-dimethoxy-4-hydroxyacetophenone	nd	nd	nd	nd	0.77 ± 0.09	0.74 ± 0.13	0.75 ± 0.08	0.71 ± 0.02
phenylacetic acid	0.32 ± 0.01	0.81 ± 0.10	5.34 ± 0.75	5.75 ± 0.28	nd	nd	nd	nd
4-hydroxyphenylacetic acid	nd	nd	nd	nd	nd	nd	4.51 ± 0.56	5.52 ± 0.28
3, 4-dihydroxyphenylacetic acid (Homoprotocatechuic acid)	nd	nd	nd	nd	19.79 ± 2.51	20.28 ± 1.07	22.07 ± 1.76	20.31 ± 0.41
indole-3-acetic acid	0.08 ± 0.04	nd	nd	0.12 ± 0.01	0.37 ± 0.02	0.37 ± 0.01	0.51 ± 0.03	0.46 ± 0.02
indole-3-carboxylic acid	1.28 ± 0.34	1.37 ± 0.41	1.32 ± 0.14	1.67 ± 0.24	2.37 ± 0.40	2.50 ± 0.23	2.71 ± 0.09	2.44 ± 0.24
indole-4-propionic acid	nd	nd	nd	nd	0.14 ± 0.01	0.14 ± 0.01	0.14 ± 0.01	nd
Chlorogenic acid	0.07 ± 0.12	nd	nd	nd	0.63 ± 0.11	0.69 ± 0.16	0.57 ± 0.12	0.35 ± 0.02
3-hydroxymandelic acid	3.98 ± 1.45	5.03 ± 0.17	4.48 ± 0.11	4.87 ± 0.67	nd	nd	nd	nd
3, 4-dihydroxymandelic acid	0.63 ± 0.07	0.40 ± 0.24	0.26 ± 0.12	0.40 ± 0.33	nd	nd	nd	nd
4-hydroxy-3-methoxy-mandelic acid	0.97 ± 0.09	0.86 ± 0.19	nd	nd	nd	nd	nd	nd
phenyllactic acid	nd	0.05 ± 0.02	0.83 ± 0.12	0.99 ± 0.08	nd	nd	0.27 ± 0.06	0.26 ± 0.03
4-hydroxyphenyllactic acid	1.20 ± 0.46	nd	nd	nd	0.56 ± 0.15	0.50 ± 0.04	1.02 ± 0.05	0.92 ± 0.11

phenylpyruvic acid	nd	0.73 ± 0.06	1.22 ± 0.19	1.58 ± 0.05	2.65 ± 0.25	2.11 ± 0.17	2.61 ± 0.35	3.20 ± 0.33
ethylferulate	nd	nd	nd	nd	0.21 ± 0.02	0.20 ± 0.02	0.20 ± 0.01	0.20 ± 0.00
catechin	1.72 ± 1.49	2.63 ± 1.06	5.57 ± 2.65	3.95 ± 2.36	3.35 ± 1.72	10.61 ± 2.23	9.63 ± 2.35	6.26 ± 1.20
epicatechin	nd	nd	nd	nd	0.18 ± 0.32	1.35 ± 0.42	1.06 ± 0.26	0.80 ± 0.25
gallocatechin	nd	0.90 ± 0.22	0.83 ± 0.60	0.64 ± 0.27	0.20 ± 0.04	0.52 ± 0.27	0.65 ± 0.36	0.25 ± 0.07
epigallocatechin	nd	0.35 ± 0.07	0.22 ± 0.08	0.25 ± 0.12	nd	nd	nd	nd
isoliquiritigenin	0.08 ± 0.00	nd	nd	nd	nd	nd	nd	nd
naringenin	nd	nd	0.00 ± 0.01	0.01 ± 0.00	nd	nd	nd	nd
kaempferol	nd	nd	nd	nd	nd	0.15 ± 0.00	0.16 ± 0.01	0.13 ± 0.02
quercetin	0.49 ± 0.29	1.19 ± 0.21	1.44 ± 0.39	1.47 ± 0.40	0.96 ± 0.12	1.42 ± 0.20	1.34 ± 0.39	1.18 ± 0.11
quercetin-3-glucoside	0.54 ± 0.06	0.35 ± 0.06	0.33 ± 0.03	0.32 ± 0.03	0.19 ± 0.03	0.18 ± 0.04	0.18 ± 0.02	0.16 ± 0.03
taxifolin	0.31 ± 0.27	0.41 ± 0.13	0.47 ± 0.17	0.49 ± 0.10	0.62 ± 0.15	0.96 ± 0.09	1.07 ± 0.08	0.72 ± 0.11
biochanin a	0.16 ± 0.01	0.47 ± 0.04	0.47 ± 0.09	0.53 ± 0.02	nd	nd	nd	nd
luteolin	1.35 ± 0.11	3.71 ± 0.52	3.81 ± 0.76	4.42 ± 0.15	3.35 ± 0.81	3.67 ± 1.23	4.16 ± 0.38	3.89 ± 0.75
apigenin	0.41 ± 0.02	1.19 ± 0.10	1.02 ± 0.12	1.24 ± 0.16	1.21 ± 0.28	1.33 ± 0.19	1.21 ± 0.10	1.36 ± 0.17
tyrosol	0.02 ± 0.03	nd	nd	nd	nd	nd	nd	nd
hydroxytyrosol	0.18 ± 0.03	0.14 ± 0.02	0.16 ± 0.05	0.16 ± 0.00	nd	nd	0.02 ± 0.01	0.04 ± 0.01
isorhamnetin	0.22 ± 0.03	0.54 ± 0.07	0.78 ± 0.09	0.74 ± 0.02	0.41 ± 0.09	0.63 ± 0.26	0.64 ± 0.07	0.67 ± 0.06
rutin	0.21 ± 0.01	nd	nd	nd	nd	0.04 ± 0.07	nd	nd
vitexin	0.30 ± 0.25	0.18 ± 0.03	0.16 ± 0.10	0.20 ± 0.01	0.33 ± 0.14	0.25 ± 0.12	0.20 ± 0.05	0.23 ± 0.11
isovitexin	0.30 ± 0.25	0.18 ± 0.03	0.16 ± 0.10	0.20 ± 0.01	0.25 ± 0.20	0.17 ± 0.05	0.15 ± 0.01	0.10 ± 0.09
hyperoside	0.58 ± 0.12	0.32 ± 0.07	0.31 ± 0.05	0.27 ± 0.03	0.22 ± 0.03	0.20 ± 0.05	0.19 ± 0.01	0.18 ± 0.01
hesperitin	nd	nd	nd	nd	nd	nd	nd	0.01 ± 0.00
ferulic dimer 8-5c	nd	0.49 ± 0.06	0.30 ± 0.06	0.36 ± 0.04	0.01 ± 0.01	0.01 ± 0.02	nd	nd
secoisolariciresinol	0.21 ± 0.07	0.22 ± 0.01	0.18 ± 0.04	0.23 ± 0.06	0.20 ± 0.01	0.13 ± 0.01	0.19 ± 0.07	0.16 ± 0.09
syringaresinol	72.55 ± 16.63	92.09 ± 16.34	89.99 ± 13.29	95.05 ± 1.11	83.57 ± 10.53	82.53 ± 13.33	74.74 ± 5.75	84.99 ± 4.65
pinoresinol	0.27 ± 0.03	1.04 ± 0.15	1.02 ± 0.17	0.99 ± 0.12	0.83 ± 0.14	0.93 ± 0.11	1.12 ± 0.04	1.04 ± 0.06

The following compounds were not detected or bellow detection limit in all the sample analysed: 3-hydroxybenzoic acid, 3, 5-dihydroxybenzoic acid, 3-, ethoxybenzoic acid, 3, 4-dimethoxybenzoic acid, 4-methoxy-3-hydroxybenzaldehyde, 2-hydroxybenzyl alcohol , 2-hydroxycinnamic acid, 3-hydroxycinnamic acid, 3-methoxycinnamic acid, 4-methoxycinnamic acid, 3, 4-dimethoxycinnamic acid, 3, 4, 5-trimethoxycinnamic acid, 2-hydroxyphenylpropionic acid, 4-hydroxyphenylpropionic acid, 3-methoxyphenylpropionic acid, 1, 2-dihydroxybenzene, 1, 3-dihydroxybenzen, 1, 2, 3-trihydroxybenzene, 3-hydroxyphenylacetic acid, 4-methoxyphenylacetic acid , 3-methoxy-4-hydroxyphenylacetic acid, mandelic acid, 4-hydroxymandelic acid, o-Hydroxyhippuric acid, phenylpropionic acid, epigallocatechin gallate, myricetin, scopoletin, umbelliferone, 7,8-dihydroxy-6-methyl coumarin, hesperidin, quercitrin, didymin, phloridzin, formononetin, phloretin, eriocitrin, naringin, morin, genistein, neohesperidin, poncirin, daidzein, galangin, equol, fisetin, neoeriocitrin, gossypin Resveratrol,ferulic dimer 5-5, ferulic dimer 8-8c, hydrogenated ferulic dimer h5-5, ellagic acid, enterodiol, lariciresinol, hydroxymatairesinol, matairesinol, enterolactone.

Where nd: were not detected or bellow detection limit.

Table S2. The metabolites with inconsistent change as average values of concentration (μg/ml) from the three donors for the microbial metabolites. The raw (set 1) and enzyme-treated hempseed screenings (EM_1 and EC_2) set 2 and set 3, as well as their corresponding in vitro-pre-digested samples were inoculated with faecal slurries from three donors (Donor 1, 2 and 3) at 0, 24, 48 and 72 hours. Blank samples were inoculated sterile PBS without faecal slurry. Values were the mean of three donors, and each donor had three replicates.

Set 1 compound (ng/ml)	Raw_ 0h	Raw_2 4h	Raw_4 8h	Raw_7 2h	Raw_ 0h blank	Raw_7 2h blank	Raw+ivgd_ 0h	Raw+ivgd_2 4h	Raw+ivgd_4 8h	Raw+ivgd_7 2h	Raw+ivgd_ 0h blank	Raw+ivgd_7 2h blank
phenylpropionic acid	41.64	76.49	83.54	86.05	41.76	45.67	42.05	70.63	97.66	106.11	39.56	41.01
phenylacetic acid	8.51	31.68	20.38	29.17	7.30	10.53	7.75	29.70	52.12	72.81	6.98	7.32
4-hydroxyphenylacetic acid	3.62	12.99	11.08	16.35	3.53	6.91	3.57	18.02	14.60	20.07	3.30	3.70
benzoic acid	1.42	1.67	1.68	1.72	1.46	1.53	1.51	1.58	1.60	1.73	1.42	1.46
3-hydroxyphenylpropionic acid	1.07	5.41	6.03	6.68	0.63	0.77	0.95	4.86	6.31	7.56	0.60	0.63
3-hydroxyphenylacetic acid	0.56	0.62	0.72	0.92	0.47	0.62	0.51	0.53	0.59	0.76	0.48	0.51
indole 3-propionic acid	0.40	0.77	0.81	0.85	0.41	0.65	0.40	0.83	0.86	0.94	0.40	0.39
p-hydroxybenzoic acid	0.23	0.32	0.35	0.40	0.22	0.29	0.19	0.23	0.27	0.32	0.18	0.19
phenyllactic acid	0.19	0.58	0.16	0.18	0.15	0.13	0.19	0.75	0.51	0.44	0.14	0.32
1, 2-dihydroxybenzene	0.18	0.40	0.44	0.60	0.16	0.27	0.17	0.24	0.27	0.43	0.12	0.15
3-hydroxymandelic acid	0.15	0.17	0.17	0.15	0.16	0.15	0.08	0.08	0.09	0.08	0.07	0.06
2-hydroxyphenylpropionic acid	0.11	0.11	0.12	0.13	0.09	0.10	0.10	0.11	0.14	0.15	0.09	0.11
4-hydroxyphenyllactic acid	0.09	0.20	0.13	0.10	0.07	0.00	0.09	0.16	0.10	0.10	0.05	0.06

Tyrosol	0.06	0.49	0.62	0.57	0.04	0.18	0.06	0.46	0.59	0.56	0.04	0.09
Indole	0.04	0.09	0.19	0.16	0.03	0.03	0.00	0.09	0.15	0.19	0.00	0.00
gentisic acid	0.04	0.27	0.26	0.26	0.00	0.00	0.00	0.06	0.06	0.07	0.00	0.00
Indole-3-carboxylic acid	0.01	0.25	0.50	0.60	0.00	0.10	0.00	0.23	0.41	0.52	0.00	0.00
2-hydroxybenzyl alcohol	0.00	0.02	0.02	0.02	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Enterodiol	0.00	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hydroxytyrosol	0.00	0.03	0.06	0.05	0.00	0.00	0.00	0.02	0.05	0.04	0.00	0.00
4-hydroxyphenylpropionic acid	0.00	12.99	7.15	7.16	0.00	1.00	0.00	45.70	3.59	4.60	0.00	0.00
I3-Acrylic	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00
1, 3-dihydroxybenzene	0.02	0.02	0.02	0.02	0.01	0.02	0.01	0.02	0.02	0.02	0.01	0.01
deoxycholic acid	2.18	1.04	0.91	1.01	0.00	0.00	2.57	1.53	1.28	1.14	0.00	0.00
Lithocholic acid	1.11	0.42	0.60	0.55	0.28	0.18	1.00	0.64	0.69	0.62	0.00	0.00
I3-Pyruvic	0.68	0.25	0.09	0.17	0.50	0.12	0.74	0.27	0.23	0.25	0.54	1.39
protocatechuic acid	0.61	0.29	0.14	0.11	0.62	0.45	0.27	0.15	0.12	0.13	0.24	0.32
2, 3-dihydroxybenzoic acid	0.53	0.20	0.18	0.15	0.23	0.17	0.25	0.17	0.16	0.15	0.22	0.20
3-methoxy-4-hydroxyphenylpropionic acid	0.52	0.00	0.00	0.00	0.46	0.29	0.48	0.00	0.00	0.00	0.43	0.44
Indole-3- acetic acid	0.45	0.42	0.44	0.46	0.47	0.48	0.46	0.39	0.41	0.48	0.46	0.49
phenylpyruvic acid	0.36	0.11	0.04	0.02	0.31	0.21	0.37	0.11	0.04	0.03	0.33	0.68
protocatechualdehyde	0.23	0.03	0.02	0.01	0.27	0.09	0.14	0.01	0.01	0.00	0.14	0.13
3, 4-dihydroxyphenylacetic acid	0.23	0.00	0.00	0.00	0.17	0.07	0.17	0.02	0.00	0.00	0.11	0.09
Vanillic acid	0.20	0.10	0.05	0.06	0.18	0.14	0.18	0.09	0.06	0.05	0.16	0.13

3, 4, 5-trihydroxybenzoic acid	0.19	0.00	0.00	0.00	0.08	0.02	0.03	0.00	0.00	0.00	0.00	0.08
p-Hydroxybenzaldehyde	0.18	0.01	0.01	0.01	0.19	0.10	0.19	0.01	0.00	0.00	0.18	0.17
3-hydroxybenzoic acid	0.18	0.16	0.16	0.17	0.17	0.19	0.16	0.14	0.14	0.17	0.16	0.17
Syringaresinol	0.18	0.00	0.00	0.00	0.24	0.00	0.00	0.00	0.00	0.00	0.15	0.19
Vitexin/Isovitexin	0.15	0.00	0.00	0.00	0.17	0.01	0.09	0.00	0.00	0.00	0.08	0.08
ferulic acid	0.14	0.00	0.00	0.00	0.09	0.05	0.08	0.00	0.00	0.00	0.09	0.09
Catechin	0.14	0.01	0.00	0.00	0.14	0.16	0.07	0.00	0.01	0.01	0.07	0.11
Chlorogenic acid	0.14	0.00	0.00	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.01	0.00
Enterolactone	0.13	0.13	0.14	0.16	0.11	0.11	0.13	0.13	0.15	0.16	0.12	0.13
3, 5-dimethoxy-4-hydroxybenzoic acid	0.13	0.01	0.00	0.00	0.13	0.08	0.11	0.01	0.01	0.02	0.11	0.08
2, 6-dihydroxybenzoic acid	0.13	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
vanillin	0.13	0.00	0.00	0.00	0.13	0.07	0.11	0.00	0.00	0.00	0.11	0.11
Fisetin	0.08	0.06	0.07	0.06	0.06	0.07	0.07	0.06	0.06	0.06	0.06	0.06
3, 5-dimethoxy-4-hydroxybenzaldehyde	0.07	0.00	0.00	0.00	0.07	0.03	0.06	0.00	0.00	0.00	0.06	0.06
I3-Carboxaldehyde	0.06	0.03	0.02	0.02	0.06	0.03	0.06	0.03	0.02	0.03	0.06	0.06
Epicatechin	0.05	0.01	0.03	0.02	0.05	0.06	0.02	0.00	0.02	0.01	0.02	0.04
caffeic acid	0.03	0.00	0.00	0.00	0.01	0.00	0.02	0.00	0.00	0.00	0.01	0.02
Luteolin	0.03	0.00	0.00	0.00	0.01	0.00	0.02	0.00	0.00	0.00	0.00	0.01
Hyperoside	0.02	0.00	0.00	0.00	0.04	0.00	0.01	0.00	0.00	0.00	0.02	0.00
Quercetin-3-Glucoside	0.02	0.00	0.00	0.00	0.04	0.00	0.01	0.00	0.00	0.00	0.02	0.00
3-methoxy-4-hydroxyacetophenone	0.02	0.00	0.00	0.00	0.02	0.01	0.01	0.00	0.00	0.00	0.01	0.02

3, 5-dimethoxy-4-hydroxycinnamic acid	0.02	0.00	0.00	0.01	0.01	0.00	0.01	0.00	0.00	0.00	0.00	0.01
ethylferulate	0.02	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
Equol	0.02	0.01	0.01	0.01	0.01	0.01	0.02	0.01	0.01	0.01	0.02	0.02
3, 4, 5-trihydroxybenzaldehyde	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3, 5-dimethoxy-4-hydroxyacetophenone	0.01	0.00	0.00	0.00	0.01	0.01	0.01	0.00	0.00	0.00	0.01	0.01
Rutin	0.01	0.00	0.00	0.00	0.15	0.00	0.02	0.00	0.00	0.00	0.12	0.12
Quercetin	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.01
Apigenin	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Quercitrin	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Genistein	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hesperidin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01
Pinoresinol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hesperitin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Naringenin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
p-Coumaric acid	0.10	0.02	0.01	0.01	0.12	0.09	0.08	0.08	0.01	0.01	0.10	0.11
Hydrogenated Ferulic Dimer H5-5	0.06	0.06	0.06	0.06	0.04	0.04	0.06	0.06	0.06	0.06	0.04	0.04
cinnamic acid	0.06	0.01	0.02	0.03	0.00	0.00	0.01	0.02	0.05	0.08	0.00	0.00
I3-Lactic	0.02	0.01	0.00	0.02	0.01	0.01	0.02	0.02	0.00	0.03	0.01	0.06
Salicylic acid	0.32	0.30	0.30	0.26	0.28	0.26	0.20	0.19	0.19	0.18	0.19	0.17
Phloretic acid	0.10	0.05	0.11	0.13	0.07	0.22	0.10	0.10	0.13	0.15	0.07	0.07
4-methoxyphenylacetic acid	0.04	0.02	0.04	0.04	0.04	0.00	0.04	0.05	0.06	0.05	0.04	0.00
4-hydroxyacetophenone	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03

Epigallocatechin	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.02	0.00

Set 2 compound (ng/ml)	EM_1_0h	EM_1_24h	EM_1_48h	EM_1_72h	EM_1_0h blank	EM_1_72h blank	EM_1+ivgd_0h	EM_1+ivgd_24h	EM_1+ivgd_48h	EM_1+ivgd_72h	EM_1+ivgd_0h blank	EM_1+ivgd_72h blank
phenylpropionic acid	39.90	74.34	85.99	90.64	40.17	41.32	41.44	76.13	87.80	92.40	40.58	40.11
phenylacetic acid	6.90	28.48	54.06	57.69	6.94	8.72	7.26	33.78	62.41	75.85	6.98	7.25
4-hydroxyphenylacetic acid	3.53	14.66	11.70	16.35	3.43	5.04	3.49	14.87	13.07	24.22	3.48	3.52
benzoic acid	1.45	1.61	1.57	1.65	1.44	1.47	1.49	1.68	1.63	1.66	1.45	1.45
3-hydroxyphenylpropionic acid	0.93	4.99	5.63	6.62	0.59	0.69	0.91	5.03	5.92	6.39	0.60	0.62
3-hydroxyphenylacetic acid	0.47	0.56	0.56	0.79	0.49	0.63	0.50	0.58	0.68	0.70	0.48	0.55
indole 3-propionic acid	0.40	0.84	0.81	0.91	0.40	0.40	0.40	0.85	0.88	0.92	0.40	0.39
p-hydroxybenzoic acid	0.21	0.31	0.33	0.37	0.21	0.24	0.19	0.27	0.30	0.32	0.18	0.18
phenyllactic acid	0.18	1.03	0.93	0.49	0.15	0.56	0.18	0.67	0.46	0.51	0.14	0.21
1, 2-dihydroxybenzene	0.18	0.32	0.39	0.56	0.15	0.19	0.17	0.25	0.27	0.42	0.14	0.14
3-hydroxymandelic acid	0.17	0.18	0.17	0.12	0.17	0.13	0.15	0.14	0.11	0.12	0.13	0.11
2-hydroxyphenylpropionic acid	0.10	0.10	0.11	0.12	0.08	0.11	0.10	0.11	0.12	0.13	0.10	0.10
4-hydroxyphenyllactic acid	0.08	0.15	0.08	0.10	0.04	0.08	0.09	0.22	0.13	0.05	0.05	0.04
Tyrosol	0.04	0.51	0.61	0.54	0.04	0.14	0.05	0.52	0.52	0.55	0.04	0.05
Indole	0.03	0.11	0.19	0.23	0.01	0.03	0.04	0.11	0.21	0.25	0.04	0.00
gentisic acid	0.02	0.19	0.17	0.18	0.00	0.00	0.00	0.07	0.06	0.06	0.00	0.00

Indole-3-carboxylic acid	0.00	0.28	0.50	0.68	0.00	0.01	0.00	0.29	0.61	0.71	0.00	0.00
2-hydroxybenzyl alcohol	0.00	0.02	0.02	0.02	0.00	0.01	0.00	0.01	0.01	0.01	0.00	0.00
Enterodiol	0.00	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hydroxytyrosol	0.00	0.03	0.05	0.04	0.00	0.00	0.00	0.03	0.05	0.05	0.00	0.00
4-hydroxyphenylpropionic acid	0.00	24.26	6.23	8.81	0.00	0.18	0.00	24.05	5.68	8.41	0.00	0.00
I3-Acrylic	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00
1, 3-dihydroxybenzene	0.01	0.02	0.02	0.03	0.01	0.00	0.02	0.02	0.02	0.03	0.02	0.01
deoxycholic acid	2.25	1.32	1.08	0.90	0.00	0.00	2.04	1.18	0.88	0.89	0.00	0.00
Lithocholic acid	0.94	0.57	0.57	0.51	0.00	0.00	0.86	0.75	0.57	0.37	0.00	0.00
I3-Pyruvic	0.62	0.24	0.18	0.21	0.46	0.46	0.72	0.15	0.18	0.24	0.54	0.88
protocatechuic acid	0.55	0.28	0.14	0.12	0.53	0.52	0.33	0.22	0.15	0.15	0.31	0.38
2, 3-dihydroxybenzoic acid	0.28	0.18	0.16	0.14	0.23	0.20	0.25	0.18	0.14	0.14	0.23	0.20
3-methoxy-4-hydroxyphenylpropionic acid	0.47	0.00	0.00	0.01	0.44	0.43	0.46	0.00	0.00	0.00	0.44	0.44
Indole-3- acetic acid	0.46	0.45	0.46	0.52	0.46	0.93	0.46	0.44	0.47	0.51	0.47	0.49
phenylpyruvic acid	0.35	0.12	0.04	0.03	0.33	0.27	0.37	0.12	0.05	0.03	0.32	0.55
protocatechualdehyde	0.24	0.02	0.02	0.01	0.29	0.12	0.20	0.02	0.01	0.01	0.21	0.17
3, 4-dihydroxyphenylacetic acid	0.22	0.00	0.00	0.00	0.20	0.09	0.17	0.01	0.00	0.00	0.16	0.06
Vanillic acid	0.19	0.09	0.05	0.06	0.19	0.16	0.17	0.08	0.05	0.05	0.17	0.10
3, 4, 5-trihydroxybenzoic acid	0.22	0.00	0.00	0.00	0.07	0.02	0.09	0.00	0.00	0.00	0.03	0.04
p-Hydroxybenzaldehyde	0.18	0.01	0.00	0.00	0.20	0.12	0.19	0.01	0.01	0.00	0.20	0.18

3-hydroxybenzoic acid	0.17	0.15	0.15	0.16	0.17	0.19	0.16	0.15	0.15	0.16	0.16	0.16
Syringaresinol	0.20	0.00	0.00	0.00	0.19	0.15	0.18	0.00	0.00	0.00	0.19	0.22
Vitexin/Isovitexin	0.16	0.00	0.00	0.00	0.13	0.14	0.14	0.00	0.00	0.00	0.10	0.13
ferulic acid	0.11	0.00	0.00	0.00	0.10	0.07	0.09	0.00	0.00	0.00	0.09	0.09
Catechin	0.12	0.01	0.01	0.00	0.09	0.11	0.09	0.01	0.00	0.00	0.07	0.10
Chlorogenic acid	0.04	0.00	0.00	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.01	0.00
Enterolactone	0.12	0.11	0.13	0.15	0.10	0.10	0.12	0.12	0.13	0.13	0.10	0.11
3, 5-dimethoxy-4-hydroxybenzoic acid	0.12	0.02	0.01	0.02	0.12	0.10	0.12	0.01	0.00	0.00	0.11	0.07
2, 6-dihydroxybenzoic acid	0.05	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
vanillin	0.12	0.00	0.00	0.00	0.13	0.08	0.12	0.00	0.00	0.00	0.12	0.12
Fisetin	0.07	0.06	0.07	0.06	0.06	0.06	0.07	0.06	0.06	0.06	0.06	0.06
3, 5-dimethoxy-4-hydroxybenzaldehyde	0.07	0.00	0.00	0.00	0.07	0.05	0.06	0.00	0.00	0.00	0.07	0.06
I3-Carboxaldehyde	0.06	0.03	0.02	0.02	0.06	0.05	0.06	0.03	0.02	0.02	0.06	0.06
Epicatechin	0.03	0.01	0.02	0.01	0.03	0.05	0.02	0.00	0.01	0.01	0.02	0.03
caffeic acid	0.03	0.00	0.00	0.00	0.02	0.01	0.02	0.00	0.00	0.00	0.01	0.01
Luteolin	0.02	0.00	0.00	0.00	0.01	0.01	0.02	0.00	0.00	0.00	0.01	0.01
Hyperoside	0.02	0.00	0.00	0.00	0.03	0.00	0.02	0.00	0.00	0.00	0.02	0.01
Quercetin-3-Glucoside	0.02	0.00	0.00	0.00	0.03	0.00	0.02	0.00	0.00	0.00	0.02	0.01
3-methoxy-4-hydroxyacetophenone	0.02	0.00	0.00	0.00	0.01	0.01	0.02	0.00	0.00	0.00	0.01	0.02
3, 5-dimethoxy-4-hydroxycinnamic acid	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
ethylferulate	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
Equol	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00	0.01	0.01

3, 4, 5-trihydroxybenzaldehyde	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3, 5-dimethoxy-4-hydroxyacetophenone	0.01	0.00	0.00	0.00	0.01	0.01	0.01	0.00	0.00	0.00	0.01	0.01
Rutin	0.01	0.00	0.00	0.00	0.08	0.00	0.01	0.00	0.00	0.00	0.05	0.06
Quercetin	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.01
Apigenin	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
Quercitrin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Genistein	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hesperidin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pinoresinol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hesperitin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Naringenin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
p-Coumaric acid	0.09	0.04	0.01	0.01	0.12	0.08	0.09	0.03	0.01	0.01	0.10	0.10
Hydrogenated Ferulic Dimer H5-5	0.05	0.05	0.06	0.06	0.04	0.04	0.05	0.06	0.06	0.06	0.04	0.04
cinnamic acid	0.04	0.01	0.02	0.04	0.00	0.01	0.01	0.01	0.03	0.04	0.00	0.00
I3-Lactic	0.02	0.01	0.02	0.03	0.01	0.09	0.02	0.02	0.00	0.03	0.01	0.00
Salicylic acid	0.28	0.29	0.29	0.26	0.27	0.27	0.19	0.20	0.18	0.17	0.19	0.17
Phloretic acid	0.10	0.15	0.17	0.13	0.05	0.08	0.09	0.08	0.10	0.09	0.04	0.03
4-methoxyphenylacetic acid	0.03	0.04	0.05	0.03	0.03	0.02	0.04	0.05	0.05	0.01	0.04	0.01
4-hydroxyacetophenone	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Epigallocatechin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Set 3 compound (ng/ml)	EC_2_ 0h	EC_2_2 4h	EC_2_4 8h	EC_2_7 2h	EC_2_ 0h blank	EC_2_7 2h blank	EC_2+ivgd _0h	EC_2+ivgd_ 24h	EC_2+ivgd_ 48h	EC_2+ivgd_ 72h	EC_2+ivgd _0h blank	EC_2+ivgd_ 72h blank
phenylpropionic acid	41.96	69.18	80.22	83.77	41.61	41.05	41.74	66.86	95.15	96.74	40.80	41.21
phenylacetic acid	7.60	30.96	17.72	30.36	7.36	7.33	7.69	30.14	67.70	31.44	9.53	9.71
4-hydroxyphenylacetic acid	3.60	13.63	11.59	15.28	3.39	3.56	3.61	15.02	14.72	19.38	2.98	3.26
benzoic acid	1.52	1.69	1.61	1.72	1.45	1.44	1.48	1.63	1.68	1.77	1.56	1.60
3-hydroxyphenylpropionic acid	0.96	5.28	6.32	7.44	0.61	0.64	0.88	4.42	6.14	6.43	0.56	0.60
3-hydroxyphenylacetic acid	0.49	0.56	0.65	0.89	0.47	0.57	0.48	0.52	0.73	0.77	0.56	0.66
indole 3-propionic acid	0.41	0.88	0.90	1.00	0.41	0.40	0.41	0.81	0.93	0.94	0.43	0.42
p-hydroxybenzoic acid	0.23	0.30	0.32	0.36	0.22	0.22	0.19	0.25	0.30	0.33	0.19	0.19
phenyllactic acid	0.19	0.49	0.15	0.16	0.15	0.23	0.18	0.65	0.28	0.25	0.16	0.23
1, 2-dihydroxybenzene	0.17	0.34	0.39	0.58	0.15	0.15	0.15	0.23	0.25	0.39	0.13	0.14
3-hydroxymandelic acid	0.16	0.16	0.17	0.12	0.16	0.15	0.13	0.15	0.09	0.10	0.13	0.11
2-hydroxyphenylpropionic acid	0.11	0.11	0.13	0.14	0.09	0.10	0.10	0.10	0.12	0.13	0.10	0.11
4-hydroxyphenyllactic acid	0.08	0.16	0.11	0.08	0.04	0.04	0.09	0.18	0.10	0.07	0.07	0.08
Tyrosol	0.05	0.49	0.60	0.51	0.04	0.12	0.05	0.54	0.53	0.60	0.04	0.05
Indole	0.03	0.12	0.23	0.25	0.00	0.00	0.00	0.11	0.20	0.22	0.06	0.01
gentisic acid	0.08	0.20	0.19	0.20	0.06	0.06	0.00	0.04	0.06	0.04	0.00	0.00

Indole-3-carboxylic acid	0.00	0.32	0.57	0.76	0.00	0.00	0.00	0.29	0.66	0.73	0.00	0.00
2-hydroxybenzyl alcohol	0.00	0.01	0.02	0.02	0.00	0.01	0.00	0.01	0.01	0.01	0.00	0.00
Enterodiol	0.00	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hydroxytyrosol	0.00	0.03	0.04	0.04	0.00	0.00	0.00	0.02	0.04	0.05	0.00	0.00
4-hydroxyphenylpropionic acid	0.00	22.09	16.05	18.61	0.00	0.00	0.00	37.21	4.05	5.48	0.00	0.00
I3-Acrylic	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00
1, 3-dihydroxybenzene	0.01	0.02	0.02	0.02	0.02	0.00	0.01	0.01	0.02	0.03	0.01	0.02
deoxycholic acid	2.50	1.38	1.29	1.16	0.00	0.00	1.83	0.97	0.85	0.88	0.00	0.00
Lithocholic acid	1.20	0.76	0.70	0.77	0.00	0.00	0.81	0.59	0.54	0.55	0.00	0.00
I3-Pyruvic	0.71	0.23	0.18	0.24	0.52	0.37	0.78	0.33	0.18	0.24	0.67	0.59
protocatechuic acid	0.58	0.23	0.12	0.11	0.57	0.61	0.33	0.22	0.18	0.16	0.32	0.37
2, 3-dihydroxybenzoic acid	0.27	0.18	0.17	0.15	0.23	0.20	0.24	0.17	0.14	0.14	0.24	0.22
3-methoxy-4-hydroxyphenylpropionic acid	0.48	0.00	0.00	0.00	0.45	0.46	0.48	0.00	0.00	0.00	0.47	0.48
Indole-3- acetic acid	0.47	0.45	0.47	0.55	0.47	0.48	0.47	0.42	0.49	0.53	0.45	0.46
phenylpyruvic acid	0.39	0.10	0.03	0.02	0.33	0.31	0.36	0.11	0.04	0.02	0.33	0.49
protocatechualdehyde	0.26	0.02	0.02	0.01	0.27	0.16	0.20	0.02	0.01	0.01	0.21	0.18
3, 4-dihydroxyphenylacetic acid	0.21	0.00	0.00	0.00	0.18	0.10	0.14	0.00	0.00	0.00	0.19	0.06
Vanillic acid	0.20	0.10	0.06	0.06	0.19	0.19	0.18	0.07	0.05	0.05	0.17	0.15
3, 4, 5-trihydroxybenzoic acid	0.17	0.00	0.00	0.00	0.07	0.05	0.08	0.00	0.00	0.00	0.02	0.02

p-Hydroxybenzaldehyde	0.19	0.01	0.00	0.00	0.20	0.15	0.18	0.01	0.01	0.00	0.21	0.21
3-hydroxybenzoic acid	0.16	0.15	0.15	0.17	0.17	0.17	0.16	0.15	0.16	0.18	0.14	0.14
Syringaresinol	0.19	0.00	0.00	0.00	0.22	0.24	0.17	0.00	0.00	0.00	0.18	0.22
Vitexin/Isovitexin	0.16	0.00	0.00	0.00	0.17	0.16	0.15	0.00	0.00	0.00	0.10	0.13
ferulic acid	0.10	0.00	0.00	0.00	0.12	0.11	0.08	0.00	0.00	0.00	0.09	0.10
Catechin	0.10	0.00	0.00	0.00	0.11	0.16	0.08	0.01	0.00	0.00	0.07	0.09
Chlorogenic acid	0.02	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Enterolactone	0.12	0.12	0.15	0.16	0.11	0.10	0.12	0.12	0.13	0.14	0.14	0.12
3, 5-dimethoxy-4-hydroxybenzoic acid	0.12	0.02	0.00	0.00	0.12	0.10	0.12	0.01	0.00	0.00	0.12	0.09
2, 6-dihydroxybenzoic acid	0.05	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
vanillin	0.13	0.00	0.00	0.00	0.13	0.10	0.12	0.00	0.00	0.00	0.13	0.14
Fisetin	0.07	0.06	0.07	0.06	0.06	0.07	0.07	0.07	0.06	0.06	0.06	0.06
3, 5-dimethoxy-4-hydroxybenzaldehyde	0.07	0.00	0.00	0.00	0.07	0.07	0.07	0.00	0.00	0.00	0.07	0.07
I3-Carboxaldehyde	0.06	0.03	0.02	0.02	0.06	0.05	0.06	0.03	0.02	0.02	0.07	0.06
Epicatechin	0.03	0.00	0.02	0.01	0.03	0.05	0.02	0.00	0.01	0.01	0.01	0.02
caffeic acid	0.03	0.00	0.00	0.00	0.02	0.02	0.02	0.00	0.00	0.00	0.01	0.01
Luteolin	0.02	0.00	0.00	0.00	0.01	0.01	0.02	0.00	0.00	0.00	0.01	0.01
Hyperoside	0.02	0.00	0.00	0.00	0.04	0.02	0.02	0.00	0.00	0.00	0.02	0.01
Quercetin-3-Glucoside	0.02	0.00	0.00	0.00	0.03	0.02	0.02	0.00	0.00	0.00	0.02	0.01
3-methoxy-4-hydroxyacetophenone	0.02	0.00	0.00	0.00	0.01	0.02	0.01	0.00	0.00	0.00	0.01	0.02

3, 5-dimethoxy-4-hydroxycinnamic acid	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
ethylferulate	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
Equol	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.02
3, 4, 5-trihydroxybenzaldehyde	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3, 5-dimethoxy-4-hydroxyacetophenone	0.01	0.00	0.00	0.00	0.01	0.01	0.01	0.00	0.00	0.00	0.01	0.01
Rutin	0.00	0.00	0.00	0.00	0.11	0.03	0.01	0.00	0.00	0.00	0.05	0.07
Quercetin	0.01	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Apigenin	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
Quercitrin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Genistein	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hesperidin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pinoresinol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hesperitin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Naringenin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
p-Coumaric acid	0.09	0.03	0.02	0.03	0.12	0.12	0.08	0.05	0.01	0.01	0.10	0.11
Hydrogenated Ferulic Dimer H5-5	0.06	0.06	0.06	0.07	0.04	0.04	0.05	0.06	0.06	0.06	0.04	0.04
cinnamic acid	0.03	0.01	0.03	0.03	0.00	0.00	0.01	0.01	0.03	0.04	0.00	0.00
I3-Lactic	0.02	0.00	0.00	0.02	0.01	0.01	0.02	0.01	0.00	0.03	0.01	0.00
Salicylic acid	0.30	0.29	0.29	0.29	0.27	0.26	0.19	0.20	0.17	0.18	0.18	0.17
Phloretic acid	0.08	0.08	0.10	0.17	0.09	0.06	0.08	0.04	0.10	0.17	0.04	0.03
4-methoxyphenylacetic acid	0.04	0.05	0.06	0.05	0.03	0.02	0.04	0.05	0.01	0.00	0.00	0.00
4-hydroxyacetophenone	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03

Epigallocatechin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

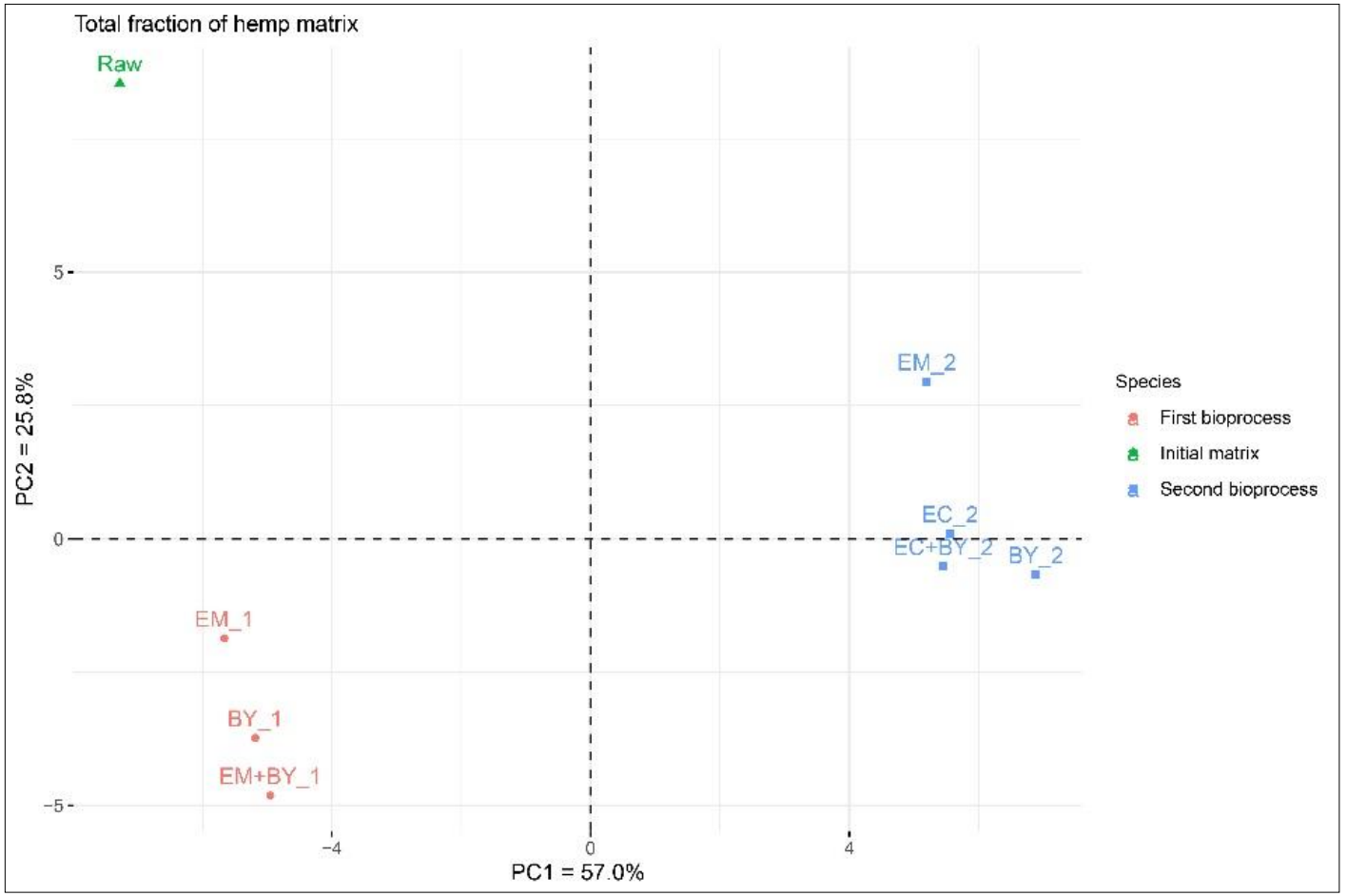

Figure S1. Principal component analysis showing discrimination between raw, first bioprocessed, and second bioprocessed hempseed screenings based on the total content (the sum of free, alkaline, and acid fractions) for all the plant metabolites measured by LC-MS/MS.