Electronic Supplementary Material (ESI) for Food & Function.

Pharmacokinetic, partial pharmacodynamic and initial safety analysis of (-)-Epicatechin in healthy volunteers

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Electronic Supplementary Material

Supplemental Table S1. Study subject characteristics

	50 mg q.d.		50 mg b.i.d.	
Characteristic	**Mean**	**SEM**	**Mean**	**SEM**
Sex (Male –n)[a]	4	44	4	50
Age (years)[b]	33	23-68	25.5	22-45
Systolic blood pressure (mmHg)	123	4.3	116.5	3
Diastolic blood pressure (mmHg)	74	2.2	67.4	2.5
Heart rate (beats per minute)	68	3.3	61	6
BMI (kg/m2)	27.2	3.7	23.2	1

Data is expressed as mean and SEM.

q.d. once a day; b.i.d, twice a day.

[a] Sex is male number and percentage.

[b] Age is median and range.

Supplemental Table S2. Laboratory data from subjects in part 2

	50 mg q.d.				50 mg b.i.d			
	Day 1		Day 5		Day 1		Day 5	
Parameters	**Mean**	**SEM**	**Mean**	**SEM**	**Mean**	**SEM**	**Mean**	**SEM**
White cell count – per mm^3	6.3	1.3	5.4	0.4	5.7	0.9	4.7	1.8
Hemoglobin – g/dL	13.4	1.3	13.1	1.6	14.3	0.67	13.8	1.3
Hematocrit - %	39	3.6	39	3.6	42	2.2	40	3.3
Mean corpuscular volume – fL	91.2	2.6	91.5	2.8	90	4.2	89.4	5
Platelet count – per mm^3	244.5	31.5	241.8	38.1	254	12.8	218	32*
Sodlium – Meq/L	140.5	1.3	140.3	0.96	141	1.9	141	2.1
Potassium - Meq/L	4.1	0.26	4.2	0.26	4.3	0.3	4.3	0.3
Bicarbonate - Meq/L	30.3	1.7	29.3	1.9	30	3.3	28	1.8
Blood urea nitrogen – mg/dL	15.3	1.3	12.8	3.3	14.3	2.5	14	2.9
Creatinine – mg/dL	0.78	0.03	0.73	0.15	0.85	0.09	0.78	0.08
Glucose – mg/dL	86.5	8.5	82.3	5.6	86.5	18.9	86	4.7
Aspartate aminotransferase – U/L	21.3	3.8	20.2	2.8	24.5	4.8	23.5	2.4
Alanine aminotransferase – U/L	16.3	6.9	14.5	4.9	17.8	3.6	18	3.2
Total Bilirubin – mg/dL	0.65	0.06	0.65	0.13	0.78	0.2	0.75	0.3
Protein – mg/dL	6.9	0.2	6.8	0.6	7.4	0.3	6.9	0.5
Alkaline Phosphatase – U/L	56	19	51	15.4	64.8	7.3	58.3	8.6[a]
Total Cholesterol – mg/L	175	49.7	172	47	144	32	140	29
Low density lipoprotein – mg/L	104	35	101	31	77	28	80	29
High density lipoprotein – mg/L	57	15	57	16	48	7	50	4
Triglycerides – mg/L	69	20	74	20	95	46	55	22

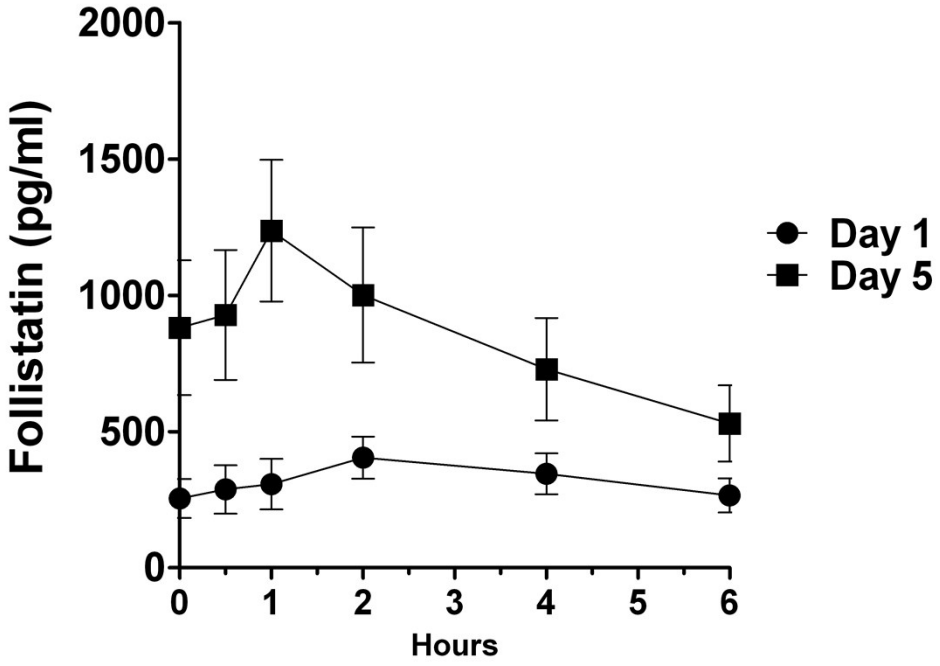
q.d., once a day; b.i.d., twice a day.

[a] $p<0.05$

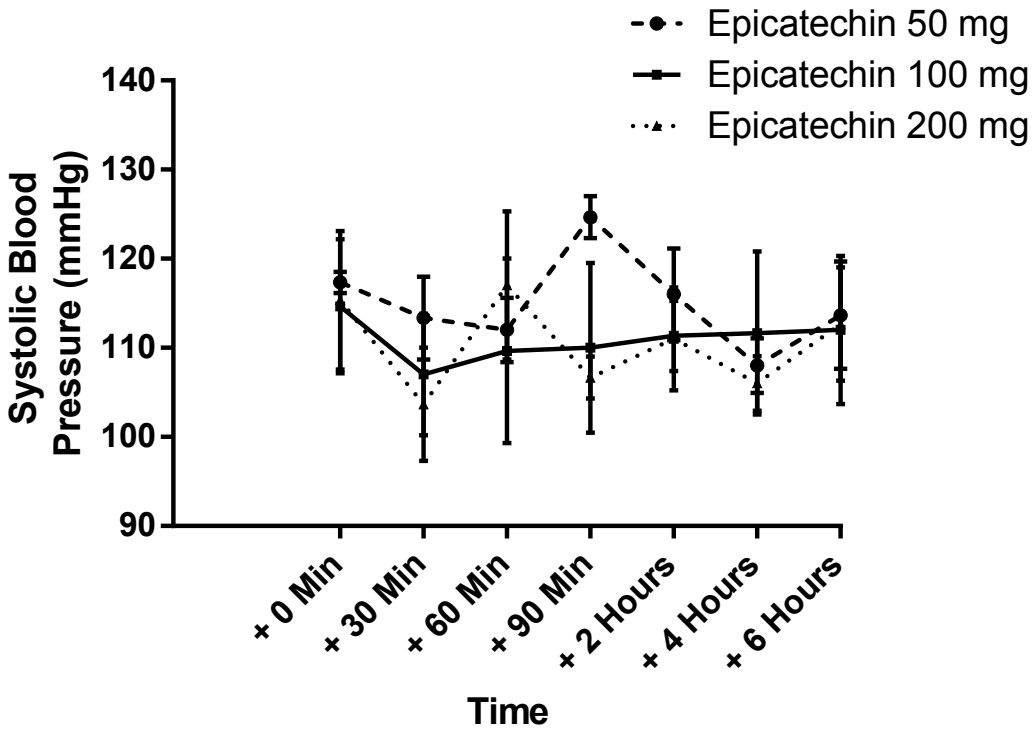
Supplemental Table S3. Pharmacokinetic study protocol

Time	Procedures performed
0	Baseline vital signs and blood obtained. (-)-Epicatechin administered
+0.5 Hours	Vital signs and blood obtained.
+1 Hour	Vital signs and blood obtained.
+1.5 Hours	Vital signs obtained
+2 Hours	Vital signs and blood obtained.
+4 Hours	Vital signs and blood obtained.
+6 Hours	Vital signs and blood obtained. Electrocardiogram performed

Supplemental Figure S1. Time course of plasma follistatin levels recorded after a single 50 mg (-)-Epicatechin ((-)-EPI) dose or repeated 5 day 50 mg b.i.d. dosing. Data are mean and SEM (n=4).



Supplemental Figure S2. Systolic blood pressure versus time following single doses of (-)-epicatechin ((-)-EPI). There were no significant differences on systolic and diastolic blood pressure (data not shown) after 50, 100 and 200 mg pure (-)-EPI administration.



Supplemental Figure S3. Systolic blood pressure versus time in subjects receiving (-)-epicatechin 50 mg q.d. and b.i.d. daily on day 1 and day 5. There were no significant differences on systolic and diastolic blood pressure (data not shown) on day 1 vs. day 5 in once daily (q.d.) and twice daily (b.i.d.) groups.